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Lipid profile pattern in pediatric overweight population with or without NAFLD in relation to IDF criteria for metabolic syndrome: a preliminary study

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Background and aims. The aim of this study is to assess the lipid profile pattern of pediatric overweight and/or obese patients with Non-Alcoholic Fatty Liver Disease (NAFLD) in relation to IDF Consensus Criteria for Metabolic Syndrome (MetS).

Material and Methods. We conducted a cross-sectional preliminary study on 45 consecutive pediatric patients. Overweight or obese children aged from 3 to 18 years were included. Standardized measurement of blood pressure and anthropometric parameters were performed. Biological evaluation included inflammatory status, lipid profile, glycemic profile, full blood count and liver function tests. Abdominal ultrasound was performed in all patients.

Results. Prevalence of MetS was 44.4%. A number of 21 patients (46.7%) had NAFLD. MetS patients had higher risk for NAFLD (OR = 9.5, 95% CI = 2.42-37.24). Also patients with positive familial history of type 2 diabetes had a 6.61 fold higher risk for NAFLD (OR = 6.61, 95% CI = 1.74-25.1). We performed a subgroup analysis in patients under ten years old. Patients under the age of ten which had both NAFLD and MetS met more frequently the hypertriglyceride criterion. After adjusting for age and MetS presence, triglyceride levels independently associated with NAFLD (adjusted R square = 0.46, unstandardized B coefficient = 34.51, 95% CI = 4.01-65.02, p = 0.02).

Conclusion. NAFLD obese patients had higher prevalence of MetS, higher BMI and particular lipid profile pattern. Triglyceride levels independently associated with NAFLD after adjusting for age and MetS presence. According to our findings we suggest early triglyceride testing (even below the age of ten) in selected patients.

Key words: obesity, dyslipidemia, NAFLD, IDF consensus criteria, metabolic syndrome, pediatric population.

INTRODUCTION

Pediatric obesity has emerged as a global pandemic in the past decades. In association with its constellation of complications is one of the most important global health burdens and issues nowadays [1]. Beside obesity, insulin resistance, metabolic syndrome and type 2 diabetes have been lately associated in the new definition of "*Diabesity*", adding more value to the overlapping image of pathophysiological pathways of these conditions [2]. In particular, there was a lack of consensus in defining the metabolic syndrome in pediatric population. The rationale of a problematic definition in pediatric population is linked to the age-related features of children development. In 2007, IDF (International Federation of Diabetes) proposes the consensus criteria for metabolic syndrome in children above the age of 10, based on the clustering of same risk factors as in the adult definition of metabolic syndrome [3]. In parallel with the rising problem of pediatric obesity and in strong relation to metabolic syndrome comes the highly concerning problem of pediatric non-alcoholic fatty liver disease (NAFLD). According to ESPGHAN, NAFLD is the most common cause of chronic liver disease in children [4]. Overweight or obese children with NAFLD experience changes in their lipid profile, partly mirroring the insulin resistance pattern. This atherogenic lipid profile displays low High-Density-Lipoprotein Cholesterol (HDL-C) levels and elevated Triglyceride (TG) serum levels. Atherogenic lipid profile can also be outlined by a couple of markers like Non-HDL Cholesterol (defined as the subtraction of the HDL-C value from the Total Cholesterol Value) and TG to HDL-C Ratio [5]. Non-HDL Cholesterol expresses all atherogenic lipid particles. TG to HDL-Cholesterol ratio is an indirect marker of insulin resistance. All these are considered better markers of cardiometabolic risk factors compared to classic evaluation of serum lipid profile [6, 7].

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The aim of this study was to assess the lipid profile pattern of pediatric overweight and/or obese patients with NAFLD in relation to IDF Consensus Criteria for Metabolic Syndrome in Children and Adolescents.

MATERIALS AND METHODS

SUBJECTS AND STUDY DESIGN

We conducted a cross-sectional study on 45 consecutive pediatric patients who attended between January to September 2017 the National Institute for Mother and Child Health "Alessandrescu-Rusescu", Bucharest. In this study were included only overweight or obese children aged from 3 to 18 years. Overweight was defined as a Body Mass Index (BMI) greater than the 85th percentile for gender and age and obesity as a BMI above the 95th centile for gender and age. Patients who had genetic traits, endocrine disorders or other causes of hepatocytolysis (infectious hepatitis, medication toxicity, celiac disease, Wilson's disease, Hemochromatosis, alpha-1 antitrypsin deficiency) were excluded from the study.

ANTHROPOMETRY AND BIOCHEMICAL EVALUATION

Anthropometric evaluation was recorded in all patients. It included the standardized measurement of height, weight, waist circumference, mid arm circumference and the calculation of BMI and of Waist to Height Ratio (WtHR). All those values were plotted on CDC growth charts and reported also as percentiles for gender and age [8-10]. Also, every patient underwent a standardized measurement of blood pressure. High blood pressure was defined as either a systolic or diastolic blood pressure with a value above the 95th percentile for age, gender and height. All standardized measurements of vital signs and anthropometry were conducted according to the guidance provided by «WHO STEPS surveillance manual: the WHO STEPwise approach to chronic disease risk factor surveillance / Noncommunicable Diseases and Mental Health, World Health Organization» [11].

Data about previous treatments was also recorded, as also the information regarding the familial obesity history, high blood pressure, type 2 diabetes or smoking history in parents and siblings. All patients underwent physical examination and biological investigation evaluating their inflammatory status (C – reactive protein – CRP), lipid profile (total cholesterol, LDL-Cholesterol, HDL-Cholesterol and triglycerides), glycemic profile, full blood count and liver function tests. Atherogenic lipid profile was outlined by a couple of markers like Non-HDL Cholesterol (defined as the subtraction of the HDL-C value from the Total Cholesterol Value) and TG to HDL-C Ratio. Metabolic syndrome was defined according to IDF Consensus Criteria. If the patient's age was under 10, one cannot conclude as having metabolic syndrome although IDF consensus criteria are met [3]. Nevertheless, in these subjects, the specific modified criteria were recorded separately.

LIVER ULTRASOUND AND NAFLD DIAGNOSIS

Abdominal ultrasound was performed in all patients in order to evaluate the presence of liver steatosis using the Toshiba Aplio 300 Ultrasound Machine. Fatty liver disease (NAFLD) was defined by ultrasound changes in liver-kidney contrast and vascular blurring for fatty liver and/or an elevated alanine-transaminase (ALT) level, more than twice the normal upper limit. The upper limit (95th percentile) of ALT in healthy, normal weight children is of 26 U/L for boys and 22 U/L for girls, according to Schwimmer *et al*. [12].

The Hospital Ethical Committee approved the study and the parent or legal guardian of every child signed an informed consent according to the Declaration of Helsinki.

STATISTICAL ANALYSIS

Data was expressed either as median (minimum and maximum value) or as mean ± standard deviation and nominal variables were presented as percentages. In order to assess association between data, non-parametrical tests were used due to small sample size. Chi-square test was used to determine association between nominal variables. Correlation analysis was performed using Spearman non-parametric test. Multivariate linear regression with triglyceride and HDL levels as dependent variables was performed in order to adjust for possible confounders (age). All data were analyzed using SPSS Version 16 for Windows.

RESULTS

A total of 45 patients were included (17 boys, 37.8%, 28 girls 62.2%), having a median age of 10 years (minimum 3 years – maximum 17 years). Prevalence of Metabolic syndrome was 44.4% (20 patients).

A number of 21 patients (46.7%) had NAFLD. All patients' characteristics are presented in Table 1.

A number of 22 patients were below the age of ten and 8 of them met all the criteria needed to diagnose metabolic syndrome according to IDF, despite the age. 12 patients from the "above 10 years old" subgroup met all the criteria for metabolic syndrome.

Table 1
Patients' characteristics

Variable	Value (n = 45)
Gender (male, %)	17 (37.8%)
Age (years)	10 (3-17) *
Weight (adjusted for age and gender percentile)	97^{th} Percentile (85^{th} - 99^{th})*
Waist circumference (adjusted for age and gender percentile)	95^{th} Percentile (75^{th} - 99^{th})*
Mid arm circumference (adjusted for age and gender percentile)	95^{th} Percentile (25^{th} - 99^{th})*
BMI (kg/m^2)	26.1 ± 5.6 **
BMI (adjusted for age and gender percentile)	98^{th} Percentile (85^{th} - 99^{th})*
BMI Z-score	2.02 ± 0.45 **
WtHR	59.1 (50-78.2)*
NAFLD (n, %)	21 (46.7%)
HTA (n, %)	20 (44.4%)
Total Cholesterol (mg/dL)	169 (115-228)*
LDL-cholesterol (mg/dL)	101 (51-156)*
HDL-cholesterol (mg/dL)	39 (19-70)*
Triglyceride (mg/dL)	104 (36-251)*
Non-HDL Cholesterol (mg/dL)	128 (67-188)*
Triglyceride to HDL Ratio	2.73 (0.71-8.58)*
CRP (mg/dL)	0.3 (0.03-5.06)*
A jèune glucose level (mg/dL)	87 (62-150)*
AST (UI/L)	24 (13-83)*
ALT (UI/L)	29 (18-224)*
Falc (UI/L)	300 (74-470)*
Uric acid (mg/dL)	4.8 (2.0-6.9)*
Metabolic syndrome – all criteria met (n, %)	20 (44.4%)
Obese (n, %)	39 (86.7%)

(BMI = Body Mass Index, WtHR = Waist to Height Ratio, NAFLD = Non-Alcoholic Fatty Liver Disease, HTA = Arterial Hypertension, LDL = Low Density Lipoprotein, HDL = High Density Lipoprotein, AST = aspartate aminotransferase, ALT = alanine aminotransferase, Falc = alkaline phosphatase)
*Data presented as median (Minimum – Maximum)
**Data presented as mean ± standard deviation

COMPARISON BETWEEN OVERWEIGHT NAFLD AND NON-NAFLD PATIENTS

Twenty one patients (46.7%) had NAFLD. Comparisons between NAFLD and non-NAFLD subgroup patients are presented in Table 2. NAFLD group had significantly higher age, BMI, triglyceride values, Triglyceride to HDL-Cholesterol Ratio values and ALT levels. NAFLD subgroup also had significantly lower HDL-Cholesterol values compared to Non-NAFLD subgroup patients (Table 2). Metabolic syndrome patients had higher risk for NAFLD (OR = 9.5 with a 95% Confidence interval, CI = 2.42-37.24). Also patients with positive familial history of type two diabetes had a 6.61 fold higher risk for NAFLD (OR = 6.61 with a 95% Confidence interval, CI = 1.74-25.1).

FREQUENCY OF IDF CONSENSUS CRITERIA FOR METABOLIC SYNDROME IN OVERWEIGHT CHILDREN AND ADOLESCENTS

As the aim of the study was to assess the lipid profile pattern of pediatric overweight and/or obese patients with NAFLD in relation to IDF Consensus Criteria for Metabolic Syndrome in Children and Adolescents, these criteria are presented in Table 3. Twenty patients met the IDF criteria for Metabolic Syndrome diagnosis irrespective of their age, 15 with NAFLD and 5 without NAFLD. The most frequently met criterion of metabolic syndrome was low HDL-cholesterol value (27 patients, 60%). A significant number of patients within the NAFLD subgroup met both hypertriglyceridemia (12 patients, 57.1% *versus* 5 patients, 20.8%, p = 0.01, Fisher Exact Test) and low HDL criteria (17 patients, 81% *versus*

10 patients, 41.7%, p = 0.01, Fisher Exact Test) of the metabolic syndrome diagnosis definition proposed by IDF, irrespective of patients' age (either below or above the age of ten).

IDF criteria are usually applied after the age of ten. In order to see if there are differences of IDF criteria before or after the age of ten, we performed a subgroup analysis in patients under ten years old (22 patients), as shown in Table 4. According to IDF, eight patients under 10 years old met all the criteria established for Metabolic Syndrome diagnosis, according to IDF. Metabolic syndrome patients had higher risk for NAFLD (OR = 18, 95% Confidence interval, CI = 2.01-161.05). The most frequently met criterion in this subgroup was low HDL-cholesterol value (12 patients, 54.5%). Patients under the age of ten which had both NAFLD and Metabolic Syndrome met more frequently the hypertriglyceride criterion (6 patients, 75% *versus* 1 patient, 7.1%, p = 0.02).

Table 2
Comparisons between NAFLD and non-NAFLD subgroup patients

Variable	NAFLD (n=21)	Non-NAFLD (n = 24)	p-value
Gender (male, %)	7 (33.3%)	10 (41.7%)	0.75
Age (years)	**12 (6-17)***	**7.5 (3-15)***	**0.002**
Weight (adjusted for age and gender percentile)	97th percentile (90th - 99th)*	97th percentile (85th - 99th)*	0.23
Waist circumference (adjusted for age and gender percentile)	95th percentile (90th - 99th)*	95th percentile (75th - 99th)*	0.13
Mid arm circumference (adjusted for age and gender percentile)	95th percentile (25th - 99th)*	95th percentile (75th - 99th)*	0.56
BMI (kg/m^2)	**28.5 ± 6.5 ** **	**24.1 ± 3.9 ** **	**0.03**
BMI (adjusted for age and gender percentile)	98th (85th - 99th)*	98th (88th - 99th)*	0.62
BMI Z-score	2.01 ± 0.49 **	2.03 ± 0.42 **	0.93
WtHR	61.1 (50-78.2)*	58.6 (50-68.7)*	0.22
HTA (n, %)	12 (57.1%)	8 (33.3%)	0.14
Total Cholesterol (mg/dL)	165 (121-228)*	181 (115-210)*	0.73
LDL-Cholesterol (mg/dL)	105 (51-156)*	99 (63-156)*	0.51
HDL-Cholesterol (mg/dL)	**35 (19-61)***	**42.5 (33-70)***	**0.002**
Triglyceride (mg/dL)	**146 (56-251)***	**79 (36-195)***	**< 0.001**
Non-HDL Cholesterol (mg/dL)	128 (67-188)*	124 (79-163)*	0.56
Triglyceride to HDL Ratio	**4.03 (1.04-8.58)***	**1.89 (0.71-5)***	**< 0.001**
CRP (mg/dL)	0.27 (0.09-2.39)*	0.40 (0.03-5.06)*	0.48
A jeune glucose level (mg/dL)	89 (66-113)*	85 (62-150)*	0.23
AST (UI/L)	26 (13-83)*	23 (17-41)*	0.13
ALT (UI/L)	**44 (18-224)***	**25 (18-37)***	**0.001**
Falc (UI/L)	300 (74-470)*	304 (178-423)*	0.68
Uric acid (mg/dL)	5.1 (2.3-6.9)*	4.2 (2.0-6.3)	0.14
Familial obesity history (n, %)	20 (95.2%)	21 (87.5%)	0.23
Passive smoking history (n, %)	10 (47.6%)	14 (58.3%)	0.54
Familial Type 2 Diabetes history (n, %)	**14 (66.6%)**	**6 (25%)**	**0.006**
Familial HTA history (n, %)	8 (38%)	5 (20.8%)	0.31
Obese (n, %)	18 (85.7%)	21 (87.5%)	1.00
Metabolic syndrome – all criteria met (n, %)	**15 (71.4%)**	**5 (20.8%)**	**0.01**
Under 10 years old (n, %)	8 (38.1%)	14 (58.3%)	0.23

(BMI = Body Mass Index, WtHR = Waist to Height Ratio, NAFLD = Non-Alcoholic Fatty Liver Disease, HTA = Arterial Hypertension, LDL = Low Density Lipoprotein, HDL = High Density Lipoprotein, AST = aspartate aminotransferase, ALT= alanine aminotransferase, Falc = alkaline phosphatase). **Bolded** data represents statistically significant differences between the two groups
*Data presented as median (Minimum – Maximum)
**Data presented as mean ± standard deviation

Table 3
Frequency of IDF Consensus Criteria for Metabolic Syndrome in Children and Adolescents. (* We applied the IDF criteria irrespective of patient age, either below or over the age of ten)

Variable	Total (n = 45)	NAFLD (n = 21)	Non-NAFLD (n = 24)	p-value
Waist circumference (> 90th percentile)	45 (100%)	21 (100%)	24 (100%)	1.00
Triglyceride (> 150 mg/dL)	**17 (37.8%)**	**12 (57.1%)**	**5 (20%)**	**0.01**
HDL (< 40 mg/dL)	**27 (60%)**	**17 (81%)**	**10 (41.7)**	**0.01**
High Systolic Blood pressure (> 130 mmHg) or High Diastolic Blood pressure (> 85 mmHg)	16 (35.6%)	10 (47.6)	6 (25%)	0.13
Fasting glucose > 100 mg/dL	8 (17.8%)	5 (23.8%)	3 (12.5%)	0.44

HDL = High Density Lipoprotein. **Bolded** data represents statistically significant differences between the two groups

Table 4
Subgroup analysis of IDF Criteria in patients under 10 years

Variable	Total (n = 22)	NAFLD (n = 8)	Non-NAFLD (n = 14)	p-value
Waist circumference (> 90th percentile)	22 (100%)	8 (100%)	14 (100%)	1.00
Triglyceride (> 150 mg/dL)	**7 (31.8%)**	**6 (75%)**	**1 (7.1%)**	**0.02**
HDL (<40 mg/dL)	12 (54.5%)	6 (75%)	6 (42.9%)	0.2
High Systolic Blood pressure (> 130 mmHg) or High Diastolic Blood pressure (> 85 mmHg)	8 (36.4%)	4 (50%)	4 (28.6%)	0.38
Fasting glucose > 100 mg/dL	4 (18.2%)	1 (12.5%)	3 (21.4%)	1.00
Metabolic syndrome – all criteria met (n, %)*	**8 (36.4%)**	**6 (75%)**	**2 (14.3%)**	**0.008**
Obese (n, %)	**19 (86.4%)**	**5 (62.5%)**	**14 (100%)**	**0.03**

HDL = High Density Lipoprotein. **Bolded** data represents statistically significant differences between the two groups (* We applied the IDF criteria irrespective of patient age)

CORRELATIONS AND MULTIVARIATE ANALYSIS

Age positively correlated with triglyceride values ($r = 0.30$, $p = 0.04$), with uric acid levels ($r = 0.50$, $p = 0.003$) and with Triglyceride to HDL-Cholesterol Ratio ($r = 0.31$, $p = 0.03$).

The percentile of waist circumference and percentile of mid arm circumference were positively correlated with Waist to Height Ratio ($r = 0.75$, $p < 0.001$, respectively $r = 0.59$, $p < 0.001$).

After adjusting for age and Metabolic Syndrome presence, triglyceride levels independently associated with NAFLD presence (adjusted R square = 0.46, unstandardized B coefficient = 34.51, 95% Confidence Interval, CI = 4.01-65.02, $p = 0.02$). However, after adjusting for age and Metabolic Syndrome presence, HDL levels were not independently associated with NAFLD presence (data not shown).

DISCUSSION

According to IDF Consensus Criteria, prevalence of Metabolic Syndrome in overweight and obese children in our study was high (44.4%). We used IDF Consensus Criteria for Metabolic Syndrome in Children and Adolescents because, according to previous findings, they are the best predictor for NAFLD [13]. In our study, Metabolic Syndrome patients had higher risk for NAFLD (OR = 9.5 with a 95% Confidence interval, CI = 2.42-37.24), as acknowledged by previous studies [13].

In our study, NAFLD patients had higher age, higher triglyceride, AST, ALT levels, very high triglyceride to HDL ratio, tendency to hyperuricemia and lower HDL levels when compared with non-NAFLD overweight and obese patients. NAFLD subgroup also had higher percentile of weight and waist circumference. Our results were mostly consistent with previous studies. NAFLD overweight and obese patients had higher age compared to non-NAFLD patients, probably due to the fact that we included overweight and obese children aged from 3 to 18 years. Considering that liver damage is a process that evolves, it usually needs time in order to detect significant ultrasonographic and/or biochemical changes associated with fatty liver disease. Our NAFLD patients had higher ALT levels and a tendency of higher AST levels (probably due to small sample size). These findings are due to the fact that NAFLD definition used in our study was based on ultrasonographic changes and/or high transaminase (ALT) levels. Nevertheless, other studies found similar changes [4, 14]. When compared to non-NAFLD patients, NAFLD patients had higher triglyceride to HDL cholesterol ratio, similar findings with Di Bonito *et al*. [5]. In their study, Di Bonito *et al.* did not find any differences of non-HDL Cholesterol levels between NAFLD and non-NAFLD obese pediatric patients, similar with our findings. According to literature, Triglyceride to HDL-Cholesterol ratio is a powerful marker of atherogenesis induced by insulin resistance. Triglyceride to HDL-Cholesterol ratio is associated with more atherogenic lipid profile and early obesity-related cardiovascular events in adult life [15].

In adults, hyperuricemia is associated with Metabolic Syndrome. In children, hyperuricemia and NAFLD are usually associated in obese children partly due to increased fructose intake [13, 16]. Also, one recent populational Chinese study revealed that abdominal obesity, BMI percentiles and hyperuricemia are associated with suspected NAFLD after adjusting for other confounders [17].

Applying IDF Consensus Criteria for Metabolic Syndrome in Children and Adolescents revealed that NAFLD patients had higher prevalence of triglyceride and HDL criteria while blood pressure

and fasting glucose criteria were similarly distributed in NAFLD and non-NAFLD overweight patients. One study, Atabek *et al*. [13], tackled the same issue on a larger group consisting of 217 obese children comparing diagnostic criteria for Metabolic Syndrome in relation to NAFLD. Some of our findings are similar (higher weight, higher BMI and higher waist circumference in NAFLD patients) but, surprisingly, the lipid profile pattern differs. Atabek *et al*. found high Total Cholesterol with high LDL-Cholesterol levels and similar levels of triglyceride and HDL Cholesterol in NAFLD obese patients *versus* Non-NAFLD obese patients. On the other hand, we found higher triglyceride levels with lower HDL-Cholesterol levels, and similar Total Cholesterol and LDL Cholesterol in NAFLD obese patients *versus* Non-NAFLD obese patients. While these differences could come from different sample sizes of the two studies (Atabeck *et al*. had higher sample size) and from ethnic differences, they could also come due to other aspects. Firstly, one major difference between the two studies is the diagnostic criteria for NAFLD. We considered NAFLD when either ultrasonography detected liver steatosis or the patient had ALT levels more than twice the normal upper limit. The upper limit (95^{th} percentile) of ALT in healthy, normal weight children is of 26 U/L for boys and 22 U/L for girls, according to Schwimmer *et al.* [12]. According to a recent systematic review tackling NAFLD diagnosis in pediatric population [18], most studies used only liver ultrasonography for detection of fatty liver. A considerable smaller number of studies used high transaminase (ALT) levels and only one study assessed both. Using both tests in parallel, one would improve the sensitivity of the diagnosis. Secondly, Atabek *et al*. included only obese patients while we included both overweight and obese ones. We included wider range of ages (3 to 18 years old *versus* 8 to 15 years old). In addition, our findings were similar with those of the Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents that have issued a summary report [19], where it is stated that nowadays the dyslipidemic pattern in obese children shifts towards moderate to severe elevation in triglyceride level, lower HDL-cholesterol level while LDL-Cholesterol and Total Cholesterol levels remain within normal ranges [19]. Moreover, we performed multivariate analysis and after adjusting for age and Metabolic Syndrome presence, NAFLD presence independently associated with triglyceride levels (adjusted R square = 0.46, unstandardized B coefficient for NAFLD = 34.51, 95% Confidence Interval, CI = 4.01-65.02, p = 0.02, triglyceride levels were considered the dependent variables). Interestingly, after adjusting for age and Metabolic Syndrome presence, HDL-Cholesterol levels did not independently associate with NAFLD presence. All these data suggest that NAFLD overweight and obese pediatric patients met more frequently hypertriglyceridemia criterion for Metabolic Syndrome irrespective of their age.

IDF criteria apply after the age of ten. In order to see if there are differences of IDF criteria before or after the age of ten, we performed a subgroup analysis on patients under 10 years of age. The prevalence of Metabolic Syndrome in this subgroup was 36.3% (8 patients out of 22). Metabolic Syndrome patients had higher risk for NAFLD (OR = 18, 95% Confidence interval, CI = 2.01-161.05). When comparing NAFLD *versus* Non-NAFLD patients, triglyceride criterion was more prevalent in NAFLD subgroup (6 patients, 75% *versus* 1 patient, 7.1%, Fisher Exact test, p = 0.02, Table 4). More importantly NAFLD was similarly distributed in both subgroups (under 10 years 8 patients, 36.4%, > 10 years 13 patients, 56.5%) – Fisher exact Test, p = 0.23. All these data suggest that the triglyceride criterion is probably the first criterion met for Metabolic Syndrome in NAFLD patients. However, only a prospective study could answer this assumption.

We have also found that patients that had at least one first or second degree relative with the diagnosis of type 2 diabetes mellitus had a higher risk for NAFLD (OR = 6.61 with a 95% Confidence interval, CI = 1.74-25.1). This finding is similar with a study in adults that tackled family history of diabetes mellitus and that found that presence of familial history of diabetes is associated with the degree of hepatic inflammation and steatosis [20].

Of course, this study has various limitations that should be acknowledged. Firstly, it has a relatively small sample size. However, some differences between groups were noted. Secondly, it had only a cross-sectional approach. Furthermore it did not assess steatosis using liver biopsy and therefore, by using in parallel ultrasonography and biochemical tests it could have decreased specificity for NAFLD diagnosis while increasing sensitivity. Nevertheless, we consider that is more important to have a more sensitive diagnostic tool for NAFLD in order not to consider many patients as false negative and thus underestimate NAFLD population.

Future studies with a prospective approach on overweight and obese children with younger ages are warranted to establish the relationship between NAFLD and Metabolic Syndrome as it is not clear whether NAFLD is causing/is caused by Metabolic Syndrome.

In conclusion, our study confirmed previous findings and described a particular lipid pattern of overweight and obese children with NAFLD. NAFLD obese patients compared with Non-NAFLD overweight and obese patients had higher prevalence of metabolic syndrome, higher BMI and particular lipid profile pattern (low HDL-Cholesterol and high triglyceride levels with high Triglyceride to HDL-Cholesterol Ratio). Triglyceride levels independently associated with NAFLD after adjusting for age and Metabolic Syndrome. According to our findings we suggest early triglyceride testing (even below the age of ten) in selected patients (overweight and obese young children with a positive familial history for Type 2 Diabetes Mellitus). These would be beneficial in order to detect possible NAFLD or Metabolic Syndrome at younger age and even if IDF Consensus Criteria are still not yet met, a close follow-up of these patients is mandatory.

Acknowledgments. This work was conducted as part of a PhD thesis ongoing at UMF "Carol Davila", Bucharest, Romania.

Conflict of interest. The authors declare that there is no conflict of interest.

Introducere. *Scopul acestui studiu a fost de a evalua modificările profilului lipidic în cadrul pacienţilor pediatrici supraponderali şi/sau obezi cu steatoză hepatică non-alcolică (NAFLD) în legătură cu Criteriile IDF de diagnostic pentru Sindromul Metabolic la copii şi adolescenţi.*

Materiale şi Metodă. *Am implementat un studiu preliminar transversal într-un grup de 45 de pacienţi pediatrici. Copiii supraponderali sau obezi cu vârste cuprinse între 3 şi 18 ani au fost înrolaţi în studiu. Evaluarea pacienţilor a inclus măsurarea standardizată a presiunii arteriale şi a parametrilor antropometrici. Evaluarea biologică a vizat statusul inflamator, profilul lipidic, profilul glicemic, parametrii hemogramei precum şi parametrii funcţiei hepatice. Toţi pacienţii au fost evaluaţi imagistic prin ultrasonografie abdominală.*

Rezultate. *Prevalenţa sindromului metabolic a fost de 44.4%. 21 pacienţi (46.7%) au avut steatoză hepatică. Pacienţii cu sindrom metabolic au avut risc mai mare pentru NAFLD (OR = 9.5, 95% CI = 2.42-37.24). Totodată, pacienţii cu antecedente heredocolaterale de Diabet Zaharat de Tip 2 au avut un risc de 6.61 ori mai mare pentru NAFLD (OR = 6.61, 95% CI = 1.74-25.1). Am efectuat o analiză de subgroup în cadrul pacienţilor cu vârsta sub 10 ani. Pacienţii cu vârsta sub 10 ani care aveau atât steatoză hepatică cât şi criteriile necesare pentru sindrom metabolic au întrunit cu o frecvenţă mai mare criteriul de hipertrigliceridemie din definiţia sindromului metabolic. După ajustarea în funcţie de vârstă şi prezenţa sindromului metabolic, nivelul trigliceridelor a fost independent asociat cu steatoza hepatică (R^2 ajustat = 0.46, coeficientul B nestandardizat = 34.51, 95% CI = 4.01-65.02, p = 0.02).*

Concluzie. *Pacienţii obezi cu NAFLD au prevalenţă mai mare a sindromului metabolic, BMI mai mare, precum şi un profil lipidic particular. Nivelul trigliceridelor serice a fost asociat independent cu NAFLD după ajustarea în funcţie de vârstă şi prezenţa sindromului metabolic. Conform rezultatelor noastre, sugerăm necesitatea evaluării nivelului trigliceridelor serice în cazuri selecţionate, inclusiv la copilul sub 10 ani.*

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