Observational Study

Medicine®

OPEN

The gap between overweight and obesity status in children - (STROBE-compliant article)

Cristina Oana Mărginean, MD, PhD[a], Lorena Elena Meliţ, MD, PhD[a,*], Adina Huţanu, MD, PhD[b], Dana Valentina Ghiga, MD, PhD[c], Maria Oana Săsăran, MD, PhD[d]

Abstract

Overweight might represent only the early stage of obesity or it might act as a trigger of self-awareness turning into an ideal chance for preventing further obesity development.

The aim of this study was to assess the differences between overweight and obese children in terms of anthropometric, low-grade systemic inflammation, liver impairment and atherosclerotic risk.

We performed a study on 132 children aged between 5 and 18 years, divided according to the BMI into 2 groups: group 1 to 76 obese children, and group 2 to 56 overweight children, assessing anthropometric, laboratory and elastography parameters.

We obtained significantly higher values of anthropometric parameters in obese children versus overweight ones. We found higher levels of leukocytes, lymphocytes, AST, ALT, and E median ($P = .0345$, $P = .0103$, $P < .0001$, $P = .0008$ and $P < .0001$) in the obese group as compared to the overweight one. BMI was positively correlated with neutrophils, NLR, ESR, glycemia, anthropometric parameters, and E median ($P = .0007/<.0001/.0018/.0044/<.0001/<.0001/<.0001/<.0001/.0204$); and negatively with lymphocytes and HDL-cholesterol ($r = -0.2747/-0.2181$, $P = .0116/.0120$).

Our study underlined significant differences between overweight and obese children in terms of inflammatory status and liver impairment suggesting that the risk is directly related to the increase in BMI.

Abbreviations: ALT = alanine aminotransferase, AST = aspartate aminotransferase, BMI = body mass index, CBC = complete cellular blood count, Chol = cholesterol, CI = confidence interval, CRP = C -reactive protein, E = elasticity, ESR = erythrocyte sedimentation rate, HDL-chol = high-density lipoprotein cholesterol, IL-6 = interleukin-6, LDL-chol = low-density lipoprotein cholesterol, MUAC = medium upper arm circumference, NAFLD = non-alcoholic fatty liver disease, NASH = non-alcoholic steato-hepatitis, NLR = neutrophils/lymphocytes ratio, PLR = platelets/lymphocytes ratio, SD = standard deviation, TG = triglycerides, TNF-alpha = tumor necrosis factor alpha, TST = tricipital skin thickness.

Keywords: assessment, inflammatory status, liver stiffness, obesity, overweight

1. Introduction

Overweight and obesity, 2 major current public health problems worldwide are defined as excessive or abnormal fat accumulation with negative impact on human's wellbeing. According to the reports of the World Health Organization, obesity has almost tripled since 1975 with more than 1.9 billion adults diagnosed with obesity, of which over 650 million suffering from overweight.[1] The incidence of these 2 conditions increased considerably in pediatric patients affecting 40 million children below 5 years of age in 2018.[1] This report is truly alarming

Editor: Khaled Saad.

All authors have no financial relationships relevant to this article to disclose.

The informed consent was signed by all parents/caregivers on behalf of their children prior to their inclusion in the study. Each child was explained all the study steps according to the age-related level of understanding, and we obtained their assent before the inclusion in the study. The approval of the Ethics Committee of the "G.E. Palade" University of Medicine, Pharmacy, Sciences and Technology of Târgu Mureş was granted for this study (No 329/ November 17th, 2017), and the study strictly complied to the Helsinki Declaration principles.

Verbal and written informed consent was obtained from the patient's mother (legal guardian) for the publication of this case presentation.

The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

[a] Department of Pediatrics I, [b] Research Laboratory, Center for Advanced Medical and Pharmaceutical Research, [c] Department of Medical Informatics and Biostatistics, [d] Department of Pediatric III, "George Emil Palade" University of Medicine, Pharmacy, Sciences and Technology from Târgu Mureş, Gheorghe Marinescu Street No 38, Romania.

[*] Correspondence: Lorena Elena Meliţ, Department of Pediatrics I, "George Emil Palade" University of Medicine, Pharmacy, Science, and Technology of Târgu Mureş, Gheorghe Marinescu Street No 38, 540136, Romania (e-mail: lory_chimista89@yahoo.com).

How to cite this article: Mărginean CO, Meliţ LE, Huţanu A, Ghiga DV, Săsăran MO. The gap between overweight and obesity status in children - (STROBE-compliant article). Medicine 2021;100:4(e24520).

Received: 22 October 2020 / Received in final form: 9 December 2020 / Accepted: 8 January 2021

http://dx.doi.org/10.1097/MD.0000000000024520

taking into account the fact that childhood obesity persists into adulthood. It is a well-documented fact that obesity is a preventable condition and overweight might play a dichotomous role in the development of obesity. Thus, overweight might represent only the early stage of obesity or it might act as a trigger of self-awareness turning into an ideal chance for preventing further obesity development. It is also true that obesity development is determined by both genetic and environmental or "obesogenic" factors,[2] which are interrelated and the latter ones can be modified.

The burden of obesity is expressed by the wide-range of complications affecting both the quality and life length, such as cardiovascular, hepatic or metabolic ones.[3] Part of these complications were hypothesized to be a result of the well-accepted low-grade inflammatory status associated to obesity, which was also proved in pediatric patients.[4] The hypothesis that adipose tissues serves as both the trigger and contributor to systemic inflammation might be a reliable explanation for the relationship between specific organ and systemic inflammation in obesity through activation of immune cells and the inflammatory processes expressed by immune cells within different specific tissues.[3] Thus, it seems that a malfunction in terms of immune activity at the level of adipose tissue involving a transient infiltration and binding of neutrophils to the adipocytes within the abdominal fat.[5] Multiple studies showed that otherwise healthy patients with obesity express increased levels of different leukocyte subclasses and elevated inflammatory biomarkers, such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) proving the strong association between obesity and subclinical systemic inflammation independently of the age.[4,6] It was also proved that adipose tissue owns the capacity to secrete different substances required for particular biological functions among which leptin, adiponectin, resistin, interleukin-6 (IL-6) and tumor necrosis factor alpha (TNF-alpha).[7] Moreover, pre-adipocytes were also proved to contribute to an increased cytokine production.[8] Therefore, the association between obesity and low-grade systemic inflammation with further life-threatening implications is an incontestable fact.

As a result of increasing obesity incidence, non-alcoholic fatty liver disease (NAFLD) is currently considered the most frequent chronic hepatic condition, its incidence reaching up to 15% in developed countries.[9] In case of children with overweight, its prevalence varies between 2.6% to 9.6%, whereas in those with obesity it rises up to 44%.[10–12] NAFLD might have a benign course, but it can also result in non-alcoholic steatohepatitis with life-threatening complications such as liver fibrosis, cirrhosis, malignant conditions or organ failure in case of long-term obesity persistence.[13] Thus, the assessment of liver inflammation through laboratory parameters and elastography methods is essential in children with overweight and obesity for a proper management.

Atherosclerosis is a major cardiovascular risk factor whose onset was established to occur during childhood in case of children diagnosed with obesity.[14] Unfortunately, due to the lack of awareness, it usually remains undiagnosed in young ages, but it persists into adulthood.[14,15] Atherosclerotic plaques are a result of the association between increased levels of low-density lipoprotein cholesterol (LDL-chol) and low levels of high-density lipoprotein cholesterol (HDL-chol).[16] Moreover, dyslipidemia, defined as hypertriglyceridemia and low HDL-cholesterol levels might led to metabolic complications in case of obese patients.[17] Lipid profile parameters, such as total cholesterol (Chol), HDL-cholesterol, LDL-cholesterol and triglycerides must be included in the routine assessment of overweight and obese children in order to establish an early diagnosis of atherosclerosis.

The aim of this study was to assess the differences between overweight and obese children in terms of anthropometric parameters, low-grade systemic inflammatory status, liver impairment and atherosclerotic risk in order to highlight the potential opportunity provided by overweight to prevent the further development of obesity, and especially its long-term associated complications.

2. Methods

2.1. Study sample selection

We performed a prospective, cross-sectional study of 132 children aged between 5 and 18 years, admitted to a Pediatric Tertiary Hospital in Romania, from April 2017 to January 2020. Taking into account the inclusion criteria, our study sample was divided according to the body mass index (BMI) into 2 groups: group 1, comprising 76 children with obesity (BMI P ≥95 for children with obesity), and group 2, the overweight group, consisting of 56 children with BMI percentile ($P \geq 85$ and <95).[18,19] Thus, the inclusion criteria comprised overweight/obese children due to poor dietary habits, age between 5 and 18 years, with at least 1-year history of excessive weight, other-wise healthy, with no previous attempts to lose weight and who performed only routine physical activity during school and play time. The exclusion criteria were: age below 5 years, monogenic and secondary obesity, infectious pathologies, chronic diseases or other conditions with inflammatory status, children with obesity-related complications, incomplete data, and children whose parents did not sign the informed consent form. Children were either referred to our clinic for nutritional status assessment by the general practitioner or endocrinology specialist, or they were brought for a routine medical consult upon their parents'/caregivers' choice. All children were assessed on a one-day chart system as they had no complications and did not require longer hospitalization.

Initially, we performed a thorough anamnesis and clinical exam to rule out those that did not fulfill our inclusion and exclusion criteria. Afterwards, the laboratory parameters assessed in all subjects included: complete cellular blood count (CBC), ESR, liver inflammation (aspartate aminotransferase - AST and alanine aminotransferase - ALT), Cholesterol (Chol), HDL-chol, LDL-chol, triglycerides (TG), and glycemia. The neutrophils/lymphocytes (NLR) and platelets/lymphocytes ratios (PLR) were calculated from the CBC, by dividing the neutrophil count and platelet count, respectively, to the lymphocyte 1.

2.1.1. Anthropometric parameters. All anthropometric measurements were performed by a single trained person and included the following: weight (kg), height (cm), abdominal perimeter (at the mid-point between the lower rib margin and the upper iliac spina), bitrochanteric perimeter (between the 2 trochanters of the femur), medium upper arm circumference (MUAC, at the midpoint between the shoulder and elbow tips with the use of a tape measure calibrated in centimeters) and tricipital skin thickness (TST, on the posterior face of the arm, using a thickness caliper). Body weight was measured with a daily calibrated scale with a ± 10 g error. A daily calibrated pedometer was used for the assessment of height with a SD (0.1-cm error).

2.1.2. Liver stiffness. The assessment of liver stiffness or liver elasticity (E) was performed by 2D-SWE method, with a Logiq S8 General Electrics Device (General Electric Healthcare, Wauwatosa, WI, USA), using a C1–6 convex probe. The software generated a region of interest, which was positioned at approximately 2 cm under the Glisson's capsule. In order to provide correct measurements, the color map had to be over 50% homogeneous. All children were examined after a fasting period of approximately 6 hours, without sedation. The measurements for each child lasted approximately 20 minutes, being performed by a highly experienced physician with over 10 years experience in pediatric ultrasound, and 4 years in elastography.

The informed consent was signed by all parents/caregivers on behalf of their children prior to their inclusion in the study. Each child was explained all the study steps according to the age-related level of understanding, and we obtained their assent before the inclusion in the study. The approval of the Ethics Committee of the "G.E. Palade" University of Medicine, Pharmacy, Sciences and Technology of Târgu Mureş was granted for this study (No 329/November 17th, 2017), and the study strictly complied to the Helsinki Declaration principles.

2.2. Statistical analysis

The statistical analysis comprised elements of descriptive statistics such as mean, median and standard deviation, but also inferential statistics ones. The Shapiro–Wilk test was used for the determination of analyzed data series distribution. The Student *t* test (parametric test for unpaired data) and Mann–Whitney (non-parametric test for unpaired data) were used for the comparison of means and medians. The power of association between variables was measured by the Pearson correlation test. For multiple correlations we applied the Dunn's multiple comparisons test.

We chose a significance threshold of 0.05 for p value, and we used the utilitarian Graph Pad Prism trial variant for the statistical analysis.

3. Results

Our study pointed that children included in the obese group had a significantly lower mean age (10.39 ± 3.379 years) as compared to the overweight ones (12.98 ± 3.090 years) ($P < .0001$), without any difference between the gender ($P = .0261$) (Table 1). Concerning the children's area of residence, we found no difference between the 2 groups in terms of rural or urban area ($P = .6536$). Children with obesity were found to have similar birth weight, 3.301 ± 0.5347 kg, to the overweight ones, 3.351 ± 1.299 kg ($P = .4122$). The current weight was higher in the obese group (60.59 ± 22.93 kg) in comparison to the overweight 1 (57.12 ± 14.42 kg), but without statistical significance ($P = .5965$), while the height was significantly higher in the overweight group (155.9 ± 14.95 cm) vs the obese 1 (146.3 ± 19.17 cm), ($P = .0021$). Analyzing the weight of the parents, we observed

Table 1

The descriptive analysis of the demographic and laboratory parameters in the obese group vs overweight group.

Parameters	Obese group (n = 76) Mean ± SD (Median)	Overweight group (n = 56) Mean ± SD (Median)	*P* value
Age (years)	10.39 ± 3.379 (11.00)	12.98 ± 3.090 (13.00)	*<.0001
Birth weight (kg)	3.301 ± 0.5347 (3.30)	3.351 ± 1.299 (3.225)	*.4122
Current weight (kg)	60.59 ± 22.93 (59.95)	57.12 ± 14.42 (58.60)	*.5965
Height (cm)	146.3 ± 19.17 (146.5)	155.9 ± 14.95 (157.0)	.0021
Leukocytes ($10^3/\mu l$)	8244 ± 2932 (7470)	7292 ± 2046 (7320)	*.0345
Neutrophils ($10^3/\mu l$)	4545 ± 2320 (3915)	3832 ± 1561 (3690)	*.1033
Lymphocytes ($10^3/\mu l$)	2880 ± 1133 (2655)	2587 ± 1091 (2365)	*.0103
Platelets ($10^3/\mu l$)	331.6 ± 87.63 (312.0)	308.7 ± 96.43 (291.5)	*.0795
NLR	1.741 ± 0.975 (1.505)	1.641 ± 0.824 (1.510)	*.5871
PLR	0.126 ± 0.0464 (0.12)	0.129 ± 0.05237 (0.11)	*.5116
ESR (mmHg)	13.32 ± 8.999 (12.00)	11.52 ± 8.025 (9.00)	*.2042
Cholesterol (mg/dl)	161.4 ± 26.44 (159.1)	160.5 ± 33.17 (155.4)	.8657
HDL (mg/dl)	44.16 ± 10.91 (43.27)	46.70 ± 12.80 (44.67)	.2214
LDL (mg/dl)	93.04 ± 25.05 (92.20)	93.10 ± 24.86 (84.60)	*.7735
TG (mg/dl)	105.3 ± 55.57 (89.28)	111.5 ± 127.1 (88.20)	*.7161
AST (UI)	27.34 ± 23.80 (22.30)	19.49 ± 5.883 (18.30)	*<.0001
ALT (UI)	26.92 ± 43.35 (18.15)	15.56 ± 7.937 (14.65)	*.0008
Glycemia (mg/dl)	87.34 ± 10.04 (86.40)	85.18 ± 8.108 (85.00)	*.2005
BMI (kg/m^2)	27.10 ± 4.750 (26.35)	23.23 ± 2.542 (23.20)	<.0001
BMI percentile	98.00 ± 2.528 (98.50)	89.05 ± 3.159 (88.90)	*<.0001
BMI Z score	2.209 ± 0.4302 (2.20)	1.246 ± 0.1737 (1.20)	*<.0001
MUAC (cm)	29.56 ± 4.620 (29.00)	27.15 ± 3.396 (27.00)	.0008
TST (mm)	19.62 ± 6.557 (18.91)	17.69 ± 4.952 (16.50)	*.0317
Abdominal perimeter (cm)	90.22 ± 14.91 (89.00)	77.88 ± 9.848 (79.00)	<.0001
Bicoxal perimeter (cm)	90.30 ± 15.09 (89.00)	84.48 ± 10.51 (85.00)	.0103
E Median 2D-SWE (kPa)	4.25 ± 0.38 (4.24)	3.60 ± 0.412 (3.705)	*<.0001
Mother's weight (kg)	75.02 ± 14.03 (74.00)	67.88 ± 15.31 (66.00)	*.0040
Father's weight (kg)	92.74 ± 15.57 (90.50)	85.87 ± 14.37 (82.00)	*.0090

2D-SWE = 2D-Shear Wave Elastography, ALT = alanine aminotransferase, AST = aspartate aminotransferase, BMI = body mass index, CRP = C reactive protein, E = elasticity, ESR = erythrocyte sedimentation rate, HDL = high density lipoprotein, kPa = Kilo Pascal, LDL = low density lipoprotein, MUAC = medium upper arm circumference, n = number, NLR = neutrophils/lymphocytes rate, PLR = platelets/lymphocytes rate, SD = standard deviation, TG = Triglycerides, TST = tricipital skin thickness.

* Mann-Whitney test was used.

that the weight of both parents was significantly higher in case of children with obesity vs overweight ones ($P=.0040$, and $P=.0090$, respectively).

In terms of anthropometric parameters, we noticed significantly higher values of BMI percentile ($P<.0001$), BMI z score ($P<.0001$), MUAC ($P=.0008$), TST ($P=.0317$), abdominal perimeter ($P<.0001$) and bitrochanteric perimeter ($P=.0103$) in children with obesity in comparison to those with overweight. Regarding the assessed laboratory parameters, our findings revealed significantly increased levels of leukocytes, lymphocytes, AST and ALT in the obese group as compared to the overweight 1 ($P=.0345$, $P=.0103$, $P<.0001$, and $P=.0008$). Assessing the liver stiffness, we noticed that children with obesity presented significant higher values of E median by 2D-SWE (4.25 ± 0.38 kPa) as compared to the overweight ones (3.60 ± 0.412 kPa) ($P<.0001$).

The values of all parameters mentioned above are described in Table 1.

We applied the Spearman correlation test in order to identify the correlations between the variables included in the study and BMI (Table 2). Thus, we noticed a significant positive correlation (direct dependency) between BMI and neutrophils ($r=0.2929$, $P=.0007$; 95% CI: [0.13–0.44]), NLR ($r=0.3375$, $P<.0001$; 95% CI: [0.18–0.48]), ESR ($r=02733$, $P=.0018$; 95% CI: [0.10–0.43]), glycemia ($r=0.2151$, $P=.0044$; 95% CI: [0.08–0.40]), BMI z score ($r=0.4341$, $P<.0001$; 95% CI: [0.28–0.56]), MUAC ($r=0.7737$, $P<.0001$; 95% CI: [0.69; 0.83]), TST ($r=0.3739$, $P<.0001$; 95% CI: [0.22–0.51]), abdominal perimeter ($r=0.8372$, $P<.0001$; 95% CI: [0.78; 0.88]), bitrochanteric perimeter ($r=0.8144$, $P<.0001$; 95% CI: [0.75–0.87]) and E median ($r=0.2017$, $P=.0204$; 95% CI: [0.03; 0.36]). Conversely, we found a significant negative correlation (reverse dependency) for lymphocytes ($r=-0.2747$, $P=.0116$; 95% CI: [−0.43; −0.11]), and HDL-chol ($r=-0.2181$, $P=.0120$; 95% CI: [−0.38–−0.05]). No significant correlations were found for leukocyte and platelet counts, PLR, Chol, LDL cholesterol, TG, AST and ALT (Table 2).

3.1. The impact of pubertal stages on the assessed parameters

In terms of pubertal status (different in girls and boys as following: for girls prepubertal 5 to 10 years, pubertal 11 to 14 years and postpubertal 15 to 18 years, and for boys: prepubertal 5 to 11 years, pubertal 12 to 16 years and postpubertal 17 to 18 years), we observed according to the Kruskal–Wallis test a significant statistical difference for BMI ($P<.0001$) between the3 groups as following: $23.63\pm3.79\,kg/m^2$ for prepubertal status, $26.66\pm4.59\,kg/m^2$ for pubertal status and $27.55\pm3.39\,kg/m^2$ for postpubertal status. Applying the Dunn's multiple comparisons test, we observed a significant difference for BMI between prepubertal and pubertal status ($P<.01$), as well as between prepubertal and postpubertal status ($P<.001$), and between prepubertal and postpubertal status ($P<.01$).

Taking into account these 3 main age groups, we assessed the paraclinical, anthropometric and elastography parameters in obese versus overweight children.

For the prepubertal group (58 children), we found significantly higher values in obese group vs overweight groups for leukocytes ($P=.0391$), neutrophils ($P=.0153$), NLR ($P=.0089$), BMI ($P<.0001$), BMI z score ($P<.0001$), MUAC ($P=.0153$), TST ($P=.0134$), abdominal perimeter ($P=.0015$), bitrochanteric perimeter ($P=.0317$) and for E Median on 2D-SWE ($P<.0001$) (Table 3).

In case of pubertal children (55 children), we observed significantly higher values in obese group vs overweight groups for the weight ($P<.0001$), AST ($P=.0095$), ALT ($P=.0109$), BMI ($P<.0001$), BMI z score ($P<.0001$), MUAC ($P<.0001$),

Table 2

The correlations between laboratory, anthropometric parameters and BMI in the 2 group.

	BMI		
Parameters	***r* coefficient**	**95% Confidence interval**	***P* value**
Leukocytes ($10^3/\mu l$)	0.07877	−0.09406 to 0.2470	.3711
Neutrophil ($10^3/\mu l$)	0.2929	0.1270 to 0.4428	.0007
Lymphocytes ($10^3/\mu l$)	−0.2747	−0.4268 to −0.1076	.0016
Platelets ($10^3/\mu l$)	−0.09480	−0.2627 to 0.07872	.2833
NLR	0.3375	0.1754 to 0.4817	<.0001
PLR	0.08137	−0.09215 to 0.2501	.3574
ESR (mmHg)	0.2733	0.1047 to 0.4267	.0018
Cholesterol (mg/dl)	−0.1320	−0.2962 to 0.03981	.1314
HDL cholesterol (mg/dl)	−0.2181	−0.3750 to -0.04900	.0120
LDL cholesterol (mg/dl)	−0.1080	−0.2739 to 0.06410	.2177
TG (mg/dl)	−0.02962	−0.1995 to 0.1420	.7360
AST (U/L)	−0.002091	−0.1729 to 0.1689	.9810
ALT (U/L)	0.09007	−0.08211 to 0.2570	.3044
Glycemia (mg/dl)	0.2462	0.07862 to 0.4003	.0044
BMI z score	0.4341	0.2843 to 0.5633	<.0001
MUAC (cm)	0.7737	0.6943 to 0.8345	<.0001
TST (mm)	0.3739	0.2162 to 0.5126	<.0001
Abdominal perimeter (cm)	0.8372	0.7772 to 0.8820	<.0001
Bicoxal perimeter (cm)	0.8144	0.7472 to 0.8651	<.0001
E Median 2D-SWE (kPa)	0.2017	0.03185 to 0.3602	.0204

2D-SWE = 2D-Shear Wave Elastography, ALT = alanine aminotransferase, AST = aspartate aminotransferase, BMI = body mass index, E = elasticity, ESR = erythrocyte sedimentation rate, HDL = high density lipoprotein, kPa = Kilo Pascal, LDL = low density lipoprotein, MUAC = medium upper arm circumference, n = number, NLR = neutrophils/lymphocytes rate, PLR = platelets/lymphocytes rate, TG = Triglycerides, TST = tricipital skin thickness, Spearman correlation was used.

Table 3

The demographic analysis of the two groups according to the prepubertal period.

Prepubertal period (n = 58) Parameters	Obese group (n = 45) Mean ± SD (Median)	Overweight group (n = 13) Mean ± SD (Median)	*P* value
Age (years)	8.15 ± 2.195 (9.00)	8.77 ± 2.127 (9.00)	*.3605
Birth weight (kg)	3.367 ± 0.5599 (3.40)	3.299 ± 0.5404 (3.25)	.6987
Current weight (kg)	45.72 ± 13.71 (45.00)	38.60 ± 10.52 (37.20)	.0900
Height (cm)	134.41 ± 14.27 (136.0)	137.54 ± 13.07 (137.0)	.4817
Leukocytes ($10^3/\mu l$)	8358 ± 3250.8 (7905)	7174.5 ± 3079.2 (7079)	*.0391
Neutrophils ($10^3/\mu l$)	4368.41 ± 2315.4 (3760)	3024.61 ± 1387.8 (3130)	*.0153
Lymphocytes ($10^3/\mu l$)	3245.45 ± 1306.4 (3005)	3260.77 ± 1781.5 (2800)	*.5555
Platelets ($10^3/\mu l$)	341.54 ± 85.458 (319.5)	324.46 ± 83.415 (289.0)	*.4699
NLR	1.499 ± 0.892 (1.312)	1.004 ± 0.497 (0.9375)	*.0089
PLR	0.118 ± 0.0459 (0.1133)	0.1112 ± 0.0341 (0.1004)	*.5491
ESR (mm Hg)	12.32 ± 7.736 (10.50)	10.23 ± 7.362 (8.00)	*.2537
Cholesterol (mg/dl)	165.43 ± 28.94 (163.4)	166.00 ± 30.401 (161.90)	*.8085
HDL (mg/dl)	46.126 ± 10.531 (45.91)	48.71 ± 11.102 (49.57)	.4444
LDL (mg/dl)	94.038 ± 26.277 (94.15)	90.63 ± 20.415 (83.790)	*.5508
TG (mg/dl)	105.57 ± 57.117 (87.00)	88.71 ± 28.373 (88.20)	*.7162
AST (Ul)	26.02 ± 9.285 (24.40)	23.76 ± 5.919 (23.20)	*.4336
ALT (Ul)	21.17 ± 13.437 (17.90)	16.98 ± 5.531 (15.60)	*.5201
Glycemia (mg/dl)	85.35 ± 9.706 (84.60)	81.75 ± 4.456 (82.60)	.0605
BMI (kg/m^2)	24.67 ± 3.546 (24.40)	19.99 ± 1.990 (19.50)	<.0001
BMI z score	2.31 ± 0.4544 (2.20)	1.32 ± 0.1878 (1.30)	*<.0001
MUAC (cm)	26.81 ± 3.350 (27.50)	24.11 ± 3.675 (23.00)	.0153
TST (mm)	19.28 ± 5.219 (18.72)	15.35 ± 3.407 (14.76)	.0134
Abdominal perimeter (cm)	82.84 ± 10.946 (82.00)	71.69 ± 9.169 (69.00)	0.0015
Bitrochanteric perimeter (cm)	82.09 ± 11.615 (81.00)	74.46 ± 8.343 (74.00)	.0317
E Median 2D-SWE (kPa)	4.28 ± 0.3825 (4.31)	3.72 ± 0.2804 (3.77)	*<.0001
Mother's weight (kg)	73.72 ± 12.119 (74.00)	72.00 ± 13.650 (74.00)	.6620
Father's weight (kg)	96.82 ± 16.274 (98.00)	88.31 ± 17.642 (88.00)	.1084

* Test Mann–Whitney.

2D-SWE = 2D-Shear Wave Elastography, ALT = alanine aminotransferase, AST = aspartate aminotransferase, BMI = body mass index, E = elasticity, ESR = erythrocyte sedimentation rate, HDL = high density lipoprotein, kPa = Kilo Pascal, LDL = low density lipoprotein, MUAC = medium upper arm circumference, n = number, NLR = neutrophils/lymphocytes rate, PLR = platelets/lymphocytes rate, TG = Triglycerides, TST = tricipital skin thickness.

abdominal perimeter ($P < .0001$), bitrochanteric perimeter ($P < .0001$) and for E Median 2D-SWE ($P < .0001$) (Table 4).

Assessing the postpubertal group (19 children), we noticed significantly higher values in obese versus overweight group for weight ($P < .0012$), BMI ($P = .0059$), BMI z score ($P = .0002$), MUAC ($P = .0032$), abdominal perimeter ($P = .0015$), bitrochanteric perimeter ($P = .0003$) and for E Median 2D-SWE ($P = .0084$) (Table 5).

3.2. Correlations between BMI and laboratory, anthropometric and elastography parameters depending on the pubertal period

During the prepubertal period we observed a positive significant correlation between BMI and neutrophils ($r = 0.3942$, 95% CI: 1488–0.5938, $P = .0024$), NLR ($r = 0.4011$, 95% CI: 0.1569–0.5991, $P = .0020$), ESR ($r = 0.3160$, 95% CI: 0.0633–0.5327, $P = .0166$), TG ($r = 0.3231$, 95% CI: 0.0706–0.5366, $P = .0134$), ALT ($r = 0.3736$, 95% CI: 0.1275–0.5763, $P = .0039$), glycemia ($r = 0.3146$, 95% CI: 0.0612–0.5299, $P = .0162$), BMI z score ($r = 0.4927$, 95% CI: 0.2685–0.6662, $P < .0001$), MUAC ($r = 0.7729$, 95% CI: 0.6430–0.8596, $P < .0001$), TST ($r = 0.4456$, 95% CI: 0.2116–0.6313, $P = .0005$), abdominal perimeter ($r = 0.8586$, 95% CI: 0.7713–0.9142, $P < .0001$), bitrochanteric perimeter ($r = 0.8136$, 95% CI: 0.7030–0.8857, $P < .0001$) and a negative correlation with HDL ($r = -0.2807$, 95% CI: −0.5026–−0.0240, $P = .0328$) (Table 6). In children of pubertal age, we noticed a positive significant correlation between BMI and ESR ($r = 0.2900$, 95% CI: 0.0185–0.5217, $P = .0370$), AST ($r = 0.3248$, 95% CI: 0.0651–0.5434, $P = .0155$), ALT ($r = 0.2728$, 95% CI: 0.0080–0.5018, $P = .0439$), BMI z score ($r = .9470$, 95% CI: 0.9105–0.9689, $P < .0001$), MUAC ($r = 0.7248$, 95% CI: 0.5688–0.8304, $P < .0001$), TST ($r = 0.3453$, 95% CI: 0.0880–0.5594, $P = .0094$), abdominal perimeter ($r = 0.8554$, 95% CI: 0.7633–0.9134, $P < .0001$), bitrochanteric perimeter ($r = 0.7641$, 95% CI: 0.6256–0.8559, $P < .0001$), as well as E median values ($r = 0.5053$, 95% CI: 0.2771–0.6796, $P < .0001$) (Table 6). In terms of postpubertal period, we found a positive significant correlation between BMI and BMI z score ($r = 0.9788$, 95% CI: 0.9444–0.9920, $P < .0001$), MUAC ($r = 0.6347$, 95% CI: 0.2384–0.8498, $P = .0047$), abdominal perimeter ($r = 0.6689$, 95% CI: 0.2936–0.8655, $P = .0024$), bitrochanteric perimeter ($r = 0.7672$, 95% CI: 0.4679–0.9087, $P = .0002$) and E median 2D-SWE ($r = 0.4604$, 95% CI: 0.0078–0.7565, $P = .0473$). All these findings were summarized in Table 6.

4. Discussions

The reports of the WHO showed during the last decades that obesity and overweight present an increasing incidence in children independently of the age and socioeconomical level.[1] Moreover, it was proved that their prevalence tends to be higher in smaller ages.[1] Our findings are alarming proving that the obese children included in our study are significantly younger as compared to the overweight ones.

Table 4

The demographic analysis of the two groups according to the pubertal period.

Pubertal period (n = 55) Parameters	Obese group (n = 26) Mean ± SD (Median)	Overweight group (n = 29) Mean ± SD (Median)	*P* value
Age (years)	13.15 ± 1.405 (13.00)	13.14 ± 1.356 (13.00)	*.8856
Birth weight (kg)	3.27 ± 0.4896 (3.30)	3.53 ± 1.73 (3.35)	*.8994
Current weight (kg)	80.58 ± 15.457 (79.15)	60.13 ± 10.265 (57.80)	<.0001
Height (cm)	162.73 ± 10.137 (160.5)	161.24 ± 10.763 (159.0)	*.3716
Leukocytes ($10^3/\mu l$)	8031.92 ± 2714.5 (7010)	7190.34 ± 1673.8 (7370)	*.4431
Neutrophils ($10^3/\mu l$)	4740 ± 2432.8 (4005)	3774.48 ± 1495.3 (3490)	*.1190
Lymphocytes ($10^3/\mu l$)	2357.31 ± 446.98 (2415)	2402.76 ± 804.12 (2340)	*.5723
Platelets ($10^3/\mu l$)	321 ± 95.746 (304.5)	321.34 ± 105.80 (312.0)	.9900
NLR	2.051 ± 1.030 (1.700)	1.734 ± 0.8635 (1.567)	*.2347
PLR	0.141 ± 0.0483 (0.1374)	0.1448 ± 0.0612 (0.1218)	*.7809
ESR (mm Hg)	15.43 ± 10.77 (15.00)	11.86 ± 8.365 (10.00)	*.2685
Cholesterol (mg/dl)	157.62 ± 20.76 (154.75)	163.41 ± 32.59 (155.50)	.4309
HDL (mg/dl)	40.26 ± 9.427 (39.95)	45.62 ± 13.238 (43.65)	.0932
LDL (mg/dl)	93.48 ± 24.736 (96.035)	97.23 ± 25.703 (91.360)	.5844
TG (mg/dl)	112.12 ± 56.274 (96.60)	136.09 ± 171.49 (89.30)	*.6920
AST (Ul)	24.19 ± 10.263 (20.615)	18.18 ± 3.492 (17.74)	*.0095
ALT (Ul)	26.13 ± 20.823 (20.75)	16.29 ± 9.542 (14.60)	*.0109
Glycemia (mg/dl)	90.46 ± 8.437 (87.70)	86.40 ± 9.243 (87.30)	*.1695
BMI (kg/m^2)	30.28 ± 4.223 (30.10)	23.43 ± 1.380 (23.10)	<.0001
BMI z score	2.08 ± 0.3702 (2.15)	1.24 ± 0.1474 (1.20)	*<.0001
MUAC (cm)	33.58 ± 3.101 (33.00)	27.67 ± 2.857 (27.00)	<.0001
TST (mm)	19.98 ± 8.316 (20.43)	18.27 ± 5.658 (17.20)	.3737
Abdominal perimeter (cm)	101 ± 13.954 (99.00)	79.665 ± 9.335 (81.00)	<.0001
Bitrochanteric perimeter (cm)	100.65 ± 10.748 (98.00)	86.34 ± 9.567 (86.00)	<.0001
E Median 2D-SWE (kPa)	4.18 ± 0.3388 (4.18)	3.57 ± 0.4520 (3.70)	<.0001
Mother's weight (kg)	75.50 ± 14.36 (71.50)	67.38 ± 15.56 (64.00)	.0502
Father's weight (kg)	87.92 ± 12.445 (87.00)	85.52 ± 13.78 (82.00)	*.2514

* Test Mann–Whitney.

2D-SWE = 2D-Shear Wave Elastography, ALT = alanine aminotransferase, AST = aspartate aminotransferase, BMI = body mass index, E = elasticity, ESR = erythrocyte sedimentation rate, HDL = high density lipoprotein, kPa = Kilo Pascal, LDL = low density lipoprotein, MUAC = medium upper arm circumference, n = number, NLR = neutrophils/lymphocytes rate, PLR = platelets/lymphocytes rate, TG = Triglycerides, TST = tricipital skin thickness.

Adipose tissue has been proved to be not only a source of inflammation, but also a target of inflammatory processes.[5] Thus, adipose tissue owns both a synthesis function and a secretion 1, being hypothesized that the secreted products act as chemoattractants and activators of different immune cells, such as monocytes or polymorphonuclear cells.[20] It is well-accepted now that the peripheral blood of otherwise healthy overweight or obese individuals express a subclinical inflammatory status.[6] A previous study of our team showed significantly higher levels of leukocytes, platelets and lymphocytes in overweight/obese children as compared to normal weight ones.[4] It was documented that lymphocyte count reflect better the nutritional body status and general stress, while the neutrophil one is rather related to the systemic inflammation in obese patients.[21] In addition, the degree of obesity seems to be better expressed by neutrophil count.[22] Except for the CBC parameters, childhood overweight and obesity was also associated with higher levels of certain adipokines, such as leptin, IL 6 and TNF alpha, which further sustain the early-stage inflammatory status associated to obesity in pediatric patients.[23] NLR was defined as an immune response marker related to chronic inflammation associated to different pathologies, such as cardiovascular, autoimmune or infectious ones, but also complicated obesity.[21,24,25] Older studies suggested that patients with uncomplicated obesity represent a particular subgroup expressing an early stage of systemic inflammation similar to the overweight ones.[26] Contrariwise, our study found significant differences in terms of leukocytes and lymphocytes between obese and overweight children, with significantly higher levels in those with obesity. Taking into account that white blood cells were proven to be related with the development of metabolic syndrome,[27] our study might suggest that this risk increases proportionally with the accumulation of fat tissue. Moreover, a direct correlation was underlined between the increase in BMI and leukocyte, neutrophil, lymphocyte and platelet counts.[28] Our findings sustain the previously mentioned ones since we also found a positive correlation between BMI and neutrophils, NLR and ESR. Thus, we may definitely confirm the strong relationship between neutrophils and obesity degree. Moreover, we might emphasize that systemic inflammation associated to excessive weight gain is directly related to the amount of fat tissue and it definitely worsens once the BMI overpasses the limit of overweight. Taking into account the previous findings of our team in terms of childhood obesity, early inflammatory status related to pediatric obesity is an alarming proven risk factor for both short- and long-term life-threatening complications and its effective control is possible only in the context of increased awareness. Contrariwise, we noticed a significant negative correlation between BMI and lymphocytes suggesting indeed that lymphocyte count might be a better indicator of nutritional status and general stress rather than obesity severity. Despite the lack of significant difference between overweight and obese children in terms of NLR, we found a strong positive dependence between this marker and the increase in BMI suggesting that chronic inflammation is most-likely to be present in the context of obesity and not overweight. This statement is further sustained by

Table 5

The demographic analysis of the two groups according to the postpubertal period.

Postpubertal period (n = 19) Parameters	Obese group (n = 5) Mean ± SD (Median)	Overweight group (n = 14) Mean ± SD (Median)	*P* value
Age (years)	16.2 ± 0.8367 (16.00)	16.57 ± 0.7559 (17.00)	*.4523
Birth weight (kg)	2.87 ± 0.3564 (3.00)	3.03 ± 0.4894 (3.035)	.5055
Current weight (kg)	90.46 ± 9.813 (91.00)	68.06 ± 7.682 (64.95)	*.0012
Height (cm)	167.2 ± 10.941 (166.00)	162.07 ± 9.825 (159.50)	*.3542
Leukocytes ($10^3/\mu l$)	8096 ± 1887.2 (7100)	7610.14 ± 1664.8 (7335)	*.9999
Neutrophils ($10^3/\mu l$)	5225 ± 1848.8 (5445)	4701.43 ± 1499.4 (4200)	*.5052
Lymphocytes ($10^3/\mu l$)	2257.5 ± 519.5 (2450)	2344.28 ± 349.39 (2350)	*.7209
Platelets ($10^3/\mu l$)	291.75 ± 35.132 (289.0)	268 ± 80.109 (238.5)	*.3391
NLR	2.379 ± 0.807 (2.658)	2.041 ± 0.6638 (1.952)	*.4418
PLR	0.134 ± 0.0282 (0.1266)	0.1150 ± 0.0339 (0.1033)	*.1922
ESR (mm Hg)	12.40 ± 10.877 (12.00)	12.00 ± 8.339 (10.50)	*.8894
Cholesterol (mg/dl)	145.08 ± 24.41 (142.30)	149.51 ± 36.55 (148.80)	.8060
HDL (mg/dl)	46.77 ± 17.438 (43.26)	47.09 ± 13.982 (44.78)	*.8230
LDL (mg/dl)	81.754 ± 13.366 (85.38)	86.84 ± 26.86 (78.75)	*.9644
TG (mg/dl)	66.8 ± 8.297 (65.40)	81.59 ± 37.181 (72.75)	.1836
AST (Ul)	16.94 ± 2.594 (17.30)	18.26 ± 8.008 (15.25)	*.8230
ALT (Ul)	15.54 ± 4.117 (14.10)	12.72 ± 5.504 (10.60)	*.1068
Glycemia (mg/dl)	88.92 ± 17.243 (87.20)	85.84 ± 7.763 (85.70)	.7196
BMI (kg/m^2)	32.38 ± 2.620 (31.50)	25.83 ± 1.304 (25.60)	.0059
BMI z score	1.98 ± 0.2168 (1.90)	1.19 ± 0.1979 (1.10)	*.0002
TST (mm)	20.84 ± 8.386 (17.21)	18.73 ± 4.017 (17.04)	*.7750
Abdominal perimeter (cm)	100.6 ± 11.415 (101.00)	80.08 ± 9.725 (78.00)	.0015
Bicoxal perimeter (cm)	110.4 ± 10.114 (108.00)	90.35 ± 7.685 (92.50)	.0003
E Median 2D-SWE (kPa)	4.288 ± 0.5798 (4.46)	3.555 ± 0.4331 (3.54)	.0084
Mother's weight (kg)	84.20 ± 25.67 (79.00)	65.11 ± 16.52 (60.00)	*.0861
Father's weight (kg)	81.00 ± 12.450 (80.00)	84.23 ± 12.846 (82.00)	.6366

* Test Mann–Whitney.

2D-SWE = 2D-Shear Wave Elastography, ALT = alanine aminotransferase, AST = aspartate aminotransferase, BMI = body mass index, E = elasticity, ESR = erythrocyte sedimentation rate, HDL = high density lipoprotein, kPa = Kilo Pascal, LDL = low density lipoprotein, MUAC = medium upper arm circumference, n = number, NLR = neutrophils/lymphocytes rate, PLR = platelets/lymphocytes rate, TG = Triglycerides, TST = tricipital skin thickness.

the negative significant correlation between BMI and HDL suggesting that in case of proper interventions once BMI decreases, the children will no longer be exposed to this cardiovascular risk factor and in exchange they might even be protected due to a subsequent increase in HDL.

Anthropometric parameters are important indicators of fat accumulation and they have been positively correlated with weight even from the time of birth.[29] Their importance in assessing excessive weight gain was proved in different population, among which pregnant women with excessive gestational weight gain,[29] but also children with obesity.[30] Additionally, waist circumference was shown to be positively correlated with CBC parameters, among which leukocytes, lymphocytes, neutrophils, platelets and medium platelet volume,[31] suggesting a potential relationship between anthropometric parameters and obesity associated inflammatory status. Similarly, our study underlined significant differences between overweight and obese children regarding all anthropometric parameters underlining a positive correlation between these parameters and BMI.

Liver steatosis or fibrosis due to excessive weight gain is a well-defined condition since non-alcoholic fatty liver disease (NAFLD) is the most common chronic hepatopathy nowadays.[10] Despite the fact that it was shown to be associated to both overweight and obesity in children, it may be present in almost 50% of children with obesity.[11] In terms of laboratory parameters, the most constant finding that suggest liver inflammation due to obesity consists in increased levels of liver transaminases.[4] Nevertheless, these levels were found to fluctuate over time and they may be even normal in children with obesity and NAFLD or non-alcoholic steato-hepatitis (NASH)[32] suggesting that their assessment alone is not enough for clearly establishing the presence of liver inflammation and/or steatosis in patients with this nutritional status disorder.[33] Moreover, the study of Cho et al underlined that only ALT might be considered a reliable parameter of liver fibrosis assessment since it was significantly correlated with liver stiffness values measured on transient elastography.[34] Despite this fact, liver transaminases along with total direct bilirubin, fasting glucose, insulin, and lipid profile parameters remain extremely useful in patients with metabolic syndrome phenotype for diagnosing fatty liver disease.[32] The association between increased levels of TG and low HDL-chol values results in insulin resistance,[14] suggesting a clear association between obesity, dyslipidemia, liver fibrosis and metabolic syndrome. Similarly, our study revealed significantly higher levels of both liver transaminases, AST and ALT in children with obesity as compared to those with overweight. Moreover, we noticed a significant positive correlation between BMI and fasting blood glucose implying that the risk of developing insulin resistance and diabetes mellitus is directly related to the degree of obesity. As for lipid profile parameters, we found a negative correlation between BMI and HDL-chol levels indicating that atherosclerotic process might indeed occur during childhood in case of obese children sustaining the findings of Williams et al.[14] Taking into account that both increased levels of LDL-chol and low levels of HDL-chol contribute to the formation of atherosclerotic plaques,[16] our findings might hypothesize that the decrease of HDL-chol could be an early indicator of this process during childhood. Nevertheless,

Table 6

Correlation between BMI and paraclinical and anthropometric parameters.

	BMI		
Prepubertal period (n = 58) Parameters	***r* coefficient**	**95% Confidence interval**	***P* value**
Leukocytes ($10^3/\mu l$)	0.0914	−0.1734 to 0.3438	.4989
Neutrophil ($10^3/\mu l$)	0.3942	0.1488 to 0.5938	.0024
Lymphocytes ($10^3/\mu l$)	−0.2329	−0.4653 to 0.0295	.0812
Platelets ($10^3/\mu l$)	−0.1153	−0.3650 to 0.1498	.3930
NLR	0.4011	0.1569 to 0.5991	.0020
PLR	−0.0032	−0.2636 to 0.2576	.9812
ESR (mm Hg)	0.3160	0.0633 to 0.5327	.0166
Cholesterol (mg/dl)	−0.0165	−0.2736 to 0.2429	.9024
HDL cholesterol (mg/dl)	−0.2807	−0.5026 to -0.0240	.0328
LDL cholesterol (mg/dl)	−0.0838	−0.3349 to 0.1784	.5316
TG (mg/dl)	0.3231	0.0706 to 0.5366	.0134
AST (U/L)	0.0426	−0.2181 to 0.2977	.7507
ALT (U/L)	0.3736	0.1275 to 0.5763	.0039
Glycemia (mg/dl)	0.3146	0.0612 to 0.5299	.0162
BMI z score	0.4927	0.2685 to 0.6662	<.0001
MUAC (cm)	0.7729	0.6430 to 0.8596	<.0001
TST (mm)	0.4456	0.2116 to 0.6313	.0005
Abdominal perimeter (cm)	0.8586	0.7713 to 0.9142	<.0001
Bitrochanteric perimeter (cm)	0.8136	0.7030 to 0.8857	<.0001
E Median 2D-SWE (kPa)	0.1654	−0.0971 to 0.4064	.2147
	BMI		
Pubertal period (n = 55) Parameters	***r* coefficient**	**95% Confidence interval**	***P* value**
Leukocytes ($10^3/\mu l$)	0.1232	−0.1469 to 0.3763	.3701
Neutrophil ($10^3/\mu l$)	0.1798	−0.0899 to 0.4249	.1891
Lymphocytes ($10^3/\mu l$)	−0.0739	−0.3327 to 0.1953	.5920
Platelets ($10^3/\mu l$)	−0.0063	−0.2712 to 0.2595	.9638
NLR	0.1370	−0.1332 to 0.3883	.3184
PLR	−0.0094	−0.2741 to 0.2555	.9458
ESR (mmHg)	0.2900	0.01853 to 0.5217	.0370
Cholesterol (mg/dl)	−0.1351	−0.3866 to 0.1351	.3253
HDL cholesterol (mg/dl)	−0.1747	−0.4206 to 0.0951	.2021
LDL cholesterol (mg/dl)	−0.1191	−0.3727 to 0.1510	.3863
TG (mg/dl)	−0.1712	−0.4176 to 0.0987	.2114
AST (U/L)	0.3248	0.0651 to 0.5434	.0155
ALT (U/L)	0.2728	0.0080 to 0.5018	.0439
Glycemia (mg/dl)	0.1703	−0.0995 to 0.4168	.2138
BMI z score	0.9470	0.9105 to 0.9689	<.0001
MUAC (cm)	0.7248	0.5688 to 0.8304	<.0001
TST (mm)	0.3453	0.0880 to 0.5594	.0094
Abdominal perimeter (cm)	0.8554	0.7633 to 0.9134	<.0001
Bitrochanteric perimeter (cm)	0.7641	0.6256 to 0.8559	<.0001
E Median 2D-SWE (kPa)	0.5053	0.2771 to 0.6796	<.0001
	BMI		
Postpubertal period (n = 19) Parameters	***r* coefficient**	**95% Confidence interval**	***P* value**
Leukocytes ($10^3/\mu l$)	0.3275	−0.1490 to 0.6805	.1711
Neutrophil ($10^3/\mu l$)	0.3007	−0.1934 to 0.6732	.2253
Lymphocytes ($10^3/\mu l$)	0.0074	−0.4612 to 0.4727	.9768
Platelets ($10^3/\mu l$)	0.1736	−0.3193 to 0.5925	.4910
NLR	0.2554	−0.2403 to 0.6454	.3065
PLR	0.1604	−0.3314 to 0.5836	.5249
ESR (mmHg)	0.0714	−0.3957 to 0.5092	.7713
Cholesterol (mg/dl)	−0.0956	−0.5270 to 0.3750	.6971
HDL cholesterol (mg/dl)	−0.1047	−0.5336 to 0.3671	.6698
LDL cholesterol (mg/dl)	−0.1282	−0.5505 to 0.3462	.6009
TG (mg/dl)	−0.1403	−0.5590 to 0.3354	.5666
AST (U/L)	−0.0942	−0.5260 to 0.3762	.7014
ALT (U/L)	0.1625	−0.3151 to 0.5744	.5063
Glycemia (mg/dl)	−0.0061	−0.4591 to 0.4495	.9803

(*continued*)

Table 6

(continued).

Postpubertal period (n = 19) Parameters	BMI		
	r coefficient	95% Confidence interval	*P* value
BMI z score	0.9788	0.9444 to 0.9920	<.0001
MUAC (cm)	0.6347	0.2384 to 0.8498	.0047
TST (mm)	0.3365	−0.1548 to 0.6944	.1722
Abdominal perimeter (cm)	0.6689	0.2936 to 0.8655	.0024
Bitrochanteric perimeter (cm)	0.7672	0.4679 to 0.9087	.0002
E Median 2D-SWE (kPa)	0.4604	0.0078 to 0.7565	.0473

2D-SWE = 2D-Shear Wave Elastography, ALT = alanine aminotransferase, AST = aspartate aminotransferase, BMI = body mass index, E = elasticity, ESR = erythrocyte sedimentation rate, HDL = high density lipoprotein, kPa = Kilo Pascal, LDL = low density lipoprotein, MUAC = medium upper arm circumference, n = number, NLR = neutrophils/lymphocytes rate, PLR = platelets/lymphocytes rate, TG = Triglycerides, TST = tricipital skin thickness.

according to the pubertal periods, our findings revealed a significant positive association between BMI and both AST and ALT during the pubertal period, and only between BMI and ALT during both prepubertal and pubertal periods, suggesting that these periods play an important role in the occurrence of obesity associated complications, such as liver inflammation or steatosis. In terms of lipid profile parameters and glycemia, our study revealed a significant positive correlation between BMI and glycemia, as well as TG only in children of prepubertal age. Moreover, according to the same age division, the significant negative correlation between BMI and HDL-chol was found also during the prepubertal period suggesting that obesity associated risks might have an earlier onset than expected.

Despite their clear utility in assessing hepatic function, laboratory parameters are not enough for providing an accurate quantification of liver fibrosis, and they should be correlated with elastography parameters for a better assessment of fibrosis degree.[35] Elastography is an essential non-invasive method in assessing the evolution and prognosis of chronic liver conditions in children.[36] Nevertheless, concerns were raised regarding certain limitation of 2D-SWE method in terms of discrimination between low-grade fibrosis and normal liver tissue.[37] Moreover, it was also hypothesized that liver inflammation, necrosis, fatty infiltration or edema might represent possible confounders for liver stiffness measurements.[38] Thus, studies performed on adult patients underlined that liver inflammation results in higher stiffness values than those expected as a consequence of fibrosis alone.[39,40] A recent study performed on pediatric patients that aimed the same aspect concluded that liver stiffness values on transient elastography should be cautiously interpreted as an indicator of hepatic fibrosis in the setting of increased ALT.[38] On the contrary, the present study proved a significant positive correlation between BMI and elastography parameters assessed by 2D-SWE, underlining significant higher values of liver stiffness in children with obesity in comparison to those with overweight. Furthermore, this correlation persisted even after the age division of our sample during all 3 periods: prepubertal, pubertal and postpubertal, while the same positive significant correlation between BMI and ALT was noticed only during the prepubertal and pubertal ones.

Another fact worth mentioning is that multiple studies revealed important changes in liver function and morphology depending on maturation status alone underlining that liver tissue suffers important modifications in time such as increase in liver volume, asymmetric or an increase in connective tissue formation resulting in higher stiffness and viscosity properties.[41–43] The present study revealed higher values of E median in obese children as compared with overweight ones independently of the group age according to the pubertal status. Moreover, we found a positive significant correlation between BMI and elastography parameters independently of the pubertal period underlining that most-likely the changes in elastography parameters are due to excessive weight and not related to the child's age under pathological circumstances. Based on the above-mentioned findings, we feel entitled to underline the strong relationship between excessive fat accumulation and liver impairment even in children. Moreover, since both ALT and elastography parameters depend in a direct manner on BMI, overweight could be considered once more a real balance between self-awareness as a subsequent trigger for implementing weight-loss strategies, and the next stage of obesity. Thus, our findings might ruin the myth of overweight defined only as a stage for imminent obesity development.

This study has some limitations that are worth mentioning among which the relatively small sample size; the fact that we did not assess children below the age of 5 years taking into account the lack of compliance in small children that could have impaired the elastography assessment resulting in false measurements; the lack of liver biopsy for a more accurate diagnosis of liver fibrosis, but its indications are very limited in children due to the potential risks related to its invasiveness, presenting no indication in children with uncomplicated obesity, and also the fact that we were not able to assess precisely the dietary habits and diet quality in order to achieve a better perspective regarding their impact on the assessed parameters. Nevertheless, our study has multiple strengths: the complex assessment of overweight and obese children in terms of inflammatory status, liver impairment, lipid profile implying the assessment of multiple anthropometric, laboratory and elastography parameters; the pediatric age of the subjects; and the random selection of the children included in the study. Moreover, our findings were used for defining a national diagnostic protocol for obese children in order to achieve a better assessment of these patients regarding both short- and long-term complications, representing also a solid basis for proper and efficacious interventions meant to decrease the alarming incidence of this pathology in pediatric patients.

To the best of our knowledge, this is the first study that aimed to assess the differences between obese and overweight children indicating that overweight is an intermediary stage between normal weight and obesity, representing indeed an ideal opportunity for the prevention of further obesity development and its related complication since bad prognosis indicators like inflammatory and lipid profile markers, as well as liver impairment are strongly related to the increase in BMI.

5. Conclusions

Our study found significant differences in terms of inflammatory status markers expressed by significantly higher levels of leukocytes and lymphocytes in children with obesity in comparison to the overweight ones, and significant positive correlation between BMI and neutrophils, ESR and NLR. Moreover, liver steatosis due to obesity was proved by significantly higher values of liver transaminases, AST and ALT, and liver stiffness in the obese group, as well as a positive correlation between BMI and elastography parameters. Regarding lipid profile, we noticed a significant negative correlation between HDL-chol and BMI. All these findings underline that bad prognosis indicators are directly related to the increase in BMI emphasizing the real gap between overweight and obesity status in children. Nevertheless, further studies on bigger cohorts are required in order to benefit from a more complex approach of the differences between overweight and obesity in children.

Acknowledgments

We express our sincere gratitude to General Electric company for providing us the Logiq S8 device and its systems, as well as to the entire team of this company, who offered their supported.

This research was partially supported by the UEFISCDI grant: "The development of an innovative diagnostic guide of obese child through genetics, anthropometric, bioimpedance and ultrasound assessment", project number: 8159/27.07.2017 - PN-III-P4-ID-PCE-2016-0766.

Author contributions

MCO, MLE, and SMO conceptualized and designed the study, drafted the initial manuscript, and revised the manuscript.

MCO, MLE, and SMO designed the data collection instruments, collected data, carried out the initial analyses, and revised the manuscript. HA performed the laboratory analysis. GDV performed the statistical analysis.

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Conceptualization: Cristina Oana Mărginean, Maria Oana Sasaran.

Data curation: Cristina Oana Mărginean.

Formal analysis: Cristina Oana Mărginean, Maria Oana Sasaran.

Investigation: Cristina Oana Mărginean, Adina Huţanu.

Methodology: Cristina Oana Mărginean, Lorena Elena Meliţ, Adina Huţanu.

Resources: Dana Valentina Ghiga.

Software: Dana Valentina Ghiga.

Supervision: Cristina Oana Mărginean, Lorena Elena Meliţ, Maria Oana Sasaran.

Validation: Cristina Oana Mărginean.

Writing – original draft: Cristina Oana Mărginean, Lorena Elena Meliţ, Maria Oana Sasaran.

Writing – review & editing: Cristina Oana Mărginean, Lorena Elena Meliţ, Maria Oana Sasaran.

References

[1] Obesity and overweight [Internet]. [cited 2020 Dec 09]. Available from: https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight

[2] Mărginean CO, Mărginean C, Meliţ LE. New insights regarding genetic aspects of childhood obesity: a mini review. Front Pediatr 2018;6:271.

[3] Pecht T, Gutman-Tirosh A, Bashan N, et al. Peripheral blood leucocyte subclasses as potential biomarkers of adipose tissue inflammation and obesity subphenotypes in humans. Obes Rev 2014;15:322–37.

[4] Mărginean C, Meliţ L, Ghiga D, et al. Early inflammatory status related to pediatric obesity (STROBE compliant article). Front Pediatr 2019;7:241doi: 10.3389/fped.2019.00241.

[5] Elgazar-Carmon V, Rudich A, Hadad N, et al. Neutrophils transiently infiltrate intra-abdominal fat early in the course of high-fat feeding. J Lipid Res 2008;49:1894–903.

[6] Trellakis S, Rydleuskaya A, Fischer C, et al. Low adiponectin, high levels of apoptosis and increased peripheral blood neutrophil activity in healthy obese subjects. Obes Facts 2012;5:305–18.

[7] Lee B-C, Lee J. Cellular and molecular players in adipose tissue inflammation in the development of obesity-induced insulin resistance. Biochim Biophys Acta 2014;1842:446–62.

[8] Xu H, Barnes GT, Yang Q, et al. Chronic inflammation in fat plays a crucial role in the development of obesity-related insulin resistance. J Clin Invest 2003;112:1821–30.

[9] Nobili V, Vizzutti F, Arena U, et al. Accuracy and reproducibility of transient elastography for the diagnosis of fibrosis in pediatric nonalcoholic steatohepatitis. Hepatology 2008;48:442–8.

[10] Tominaga K, Kurata JH, Chen YK, et al. Prevalence of fatty liver in Japanese children and relationship to obesity. An epidemiological ultrasonographic survey. Dig Dis Sci 1995;40:2002–9.

[11] Schwimmer JB, Deutsch R, Kahen T, et al. Prevalence of fatty liver in children and adolescents. Pediatrics 2006;118:1388–93.

[12] Sartorio A, Del Col A, Agosti F, et al. Predictors of non-alcoholic fatty liver disease in obese children. Eur J Clin Nutr 2007;61:877–83.

[13] Loomba R, Sirlin CB, Schwimmer JB, et al. Advances in pediatric nonalcoholic fatty liver disease. Hepatology 2009;50:1282–93.

[14] Williams CL, Hayman LL, Daniels SR, et al. Cardiovascular health in childhood: a statement for health professionals from the Committee on Atherosclerosis, Hypertension, and Obesity in the Young (AHOY) of the Council on Cardiovascular Disease in the Young, American Heart Association. Circulation 2002;106:143–60.

[15] Baker JL, Olsen LW, Sørensen TIA. Childhood body-mass index and the risk of coronary heart disease in adulthood. N Engl J Med 2007; 357:2329–37.

[16] Shah PK. High-density lipoprotein mimetics: focus on synthetic high-density lipoprotein. Am J Cardiol 2007;100(11 A):S62–7.

[17] Sumner AE. Ethnic differences in triglyceride levels and high-density lipoprotein lead to underdiagnosis of the metabolic syndrome in black children and adults. J Pediatr 2009;155: S7.e7-11.

[18] Mantzouranis N, Pilianidis T, Douda H, et al. Comparison of international obesity taskforce cutoffs, centers for disease control and prevention growth charts, and body mass index z-score values in the prevalence of childhood obesity: the Greek obesity and lifestyle study. Pediatrics 2008;121(Supplement 2):S149–149.

[19] Defining Childhood Obesity | Overweight & Obesity | CDC [Internet]. [cited 2020 Dec 09]. Available from: https://www.cdc.gov/obesity/childhood/defining.html

[20] Fantuzzi G. Adipose tissue, adipokines, and inflammation. J Allergy Clin Immunol 2005;115:911–9. quiz 920.

[21] Bozkuş F, Dikmen N, Samur A, et al. Does the neutrophil-to-lymphocyte ratio have any importance between subjects with obstructive sleep apnea syndrome with obesity and without obesity? Tuberk Toraks 2018; 66:8–15.

[22] Atmaca H, Akbaş F, Ökten I, et al. Can neutrophil-to-lymphocyte ratio serve as an inflammatory marker in obesity? İstanbul Med J 2014;15:216–20.

[23] Mărginean CO, Meliţ LE, Huţanu A, et al. The adipokines and inflammatory status in the era of pediatric obesity. Cytokine 2020;126:154925.

[24] Doğan M, Akyel A, Bilgin M, et al. Can admission neutrophil to lymphocyte ratio predict infarct-related artery patency in st-segment elevation myocardial infarction? Clin Appl Thromb Hemost 2015; 21:172–6.

[25] Ozbay I, Kahraman C, Balikci HH, et al. Neutrophil-to-lymphocyte ratio in patients with peripheral vertigo: a prospective controlled clinical study. Am J Otolaryngol 2014;35:699–702.

[26] Vargas R, Ryder E, Diez-Ewald M, et al. Increased C-reactive protein and decreased Interleukin-2 content in serum from obese individuals with or without insulin resistance: associations with leukocyte count and insulin

and adiponectin content. Diabetes Metab Syndr 2016;10(1 Suppl 1): S34–41.
[27] Fadini GP, Marcuzzo G, Marescotti MC, et al. Elevated white blood cell count is associated with prevalence and development of the metabolic syndrome and its components in the general population. Acta Diabetol 2012;49:445–51.
[28] Furuncuoğlu Y, Tulgar S, Dogan AN, et al. How obesity affects the neutrophil/lymphocyte and platelet/lymphocyte ratio, systemic immune-inflammatory index and platelet indices: a retrospective study. Eur Rev Med Pharmacol Sci 2016;20:1300–6.
[29] Mărginean C, Mărginean CO, Iancu M, et al. The role of TGF-(1 869 T>C and PPAR (2 34 C>G polymorphisms, fat mass, and anthropometric characteristics in predicting childhood obesity at birth: a cross-sectional study according the parental characteristics and newborn's risk for child obesity (the newborns obesity's risk) NOR study. Medicine (Baltimore) 2016;95:e4265.
[30] Duicu C, Mărginean CO, Voidăzan S, et al. FTO rs 9939609 SNP is associated with adiponectin and leptin levels and the risk of obesity in a cohort of Romanian children population. Medicine (Baltimore) 2016;95: e3709.
[31] Vuong J, Qiu Y, La M, et al. Reference intervals of complete blood count constituents are highly correlated to waist circumference: should obese patients have their own "normal values?". Am J Hematol 2014;89: 671–7.
[32] Feldstein AE, Charatcharoenwitthaya P, Treeprasertsuk S, et al. The natural history of non-alcoholic fatty liver disease in children: a follow-up study for up to 20 years. Gut 2009;58:1538–44.
[33] Denzer UW, Lüth S. Non-invasive diagnosis and monitoring of liver fibrosis and cirrhosis. Best Pract Res Clin Gastroenterol 2009;23: 453–60.
[34] Cho Y, Tokuhara D, Morikawa H, et al. Transient elastography-based liver profiles in a hospital-based pediatric population in Japan. PLoS One 2015;10:e0137239.
[35] Hudert CA, Tzschätzsch H, Guo J, et al. US time-harmonic elastography: detection of liver fibrosis in adolescents with extreme obesity with nonalcoholic fatty liver disease. Radiology 2018;288:99–106.
[36] Sleman IH, Liszewski MC. Ultrasound elastography in the noninvasive diagnosis of liver disease in children: a review. Central European J Paediatr 2016;12:41–8.
[37] Özkan MB, Bilgici MC, Eren E, et al. Role of point shear wave elastography in the determination of the severity of fibrosis in pediatric liver diseases with pathologic correlations. J Ultrasound Med 2017; 36:2337–44.
[38] Raizner A, Shillingford N, Mitchell PD, et al. Hepatic inflammation may influence liver stiffness measurements by transient elastography in children and young adults. J Pediatr Gastroenterol Nutr 2017;64:512–7.
[39] Tapper EB, Cohen EB, Patel K, et al. Levels of alanine aminotransferase confound use of transient elastography to diagnose fibrosis in patients with chronic hepatitis C virus infection. Clin Gastroenterol Hepatol 2012;10:932–7.e1.
[40] Liang X-E, Chen Y-P, Zhang Q, et al. Dynamic evaluation of liver stiffness measurement to improve diagnostic accuracy of liver cirrhosis in patients with chronic hepatitis B acute exacerbation. J Viral Hepat 2011;18:884–91.
[41] Pauleau G, Sandoz B, Thollon L, et al. Anthropometric characterization of the child liver. Surg Radiol Anat 2010;32:767–75.
[42] Johnson TN, Tucker GT, Tanner MS, et al. Changes in liver volume from birth to adulthood: a meta-analysis. Liver Transpl 2005;11:1481–93.
[43] Yarpuzlu B, Ayyildiz M, Tok OE, et al. Correlation between the mechanical and histological properties of liver tissue. J Mech Behav Biomed Mater 2014;29:403–16.