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Original article

Features of the mobile pool of fatty acids (lipoproteins and free fatty acids) in adolescents with different body weights

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Abstract: *Background* — Studying the lipidome and, in particular, the mobile pool of fatty acids (FA) can provide more detailed information about the development and maintenance of excess body fat, which makes this scientific direction promising. The goal of this study was to investigate the characteristics of the mobile pool of FA, including membrane indices in adolescents with different body weights.
Methods — The study included 75 adolescents aged 10 to 17 years. The main group (n=45) included adolescents with Grade 1 and Grade 2 alimentary obesity. The control group comprised 30 healthy adolescents. The control and main groups were divided into subgroups based on gender. Anthropometric assessment included measuring height and body weight. The mobile pool of FA (lipoproteins and free fatty acids, FFA) in the blood serum was analyzed on an Agilent 7000B chromatography mass spectrometry device.
Results — Among boys, a number of indices demonstrated statistically significant changes, e.g., whole blood ω-3 index (1.335 [1.230; 1.540] % of FA) and erythrocyte membrane ω-3 index (1.620 [1.520; 1.813] % of FA). The ω-6/ω-3 FA ratio in the presence of obesity (13.310 [11.400; 16.705] % of FA) exceeded the upper limit of the laboratory reference range (2.90-13.06% of FA) in boys. The subintimal inflammatory response risk index was elevated in both groups, but was significantly higher among adolescents with normal body weight (51.320 [38.368; 57.260] % of FA and 81.450 [63.120; 210.860] % of FA, respectively). The polyunsaturated/saturated FA index demonstrated levels of 0.400 [0.375; 0.558] % of FA and 0.740 [0.630; 0.990] % of FA in the main and control groups, respectively. Among girls, a number of indices demonstrated statistically significant changes: e.g., ω-3 FA (% of saturated FA) in the obese group showed a level of 1.680 [1.365; 1.910] % of FA, ω-6 FA (% of saturated FA) also demonstrated a reduction in the presence of obesity (21.050 [19.130; 23.100] % of FA). Levels of polyunsaturated FA (% of total FA) were lower both vs. the control group and reference values (36.67-47.73% of FA): 22.380 [20.790; 24.990] % of FA and 35.460 [30.290; 42.950] % of FA, respectively. Saturated FA (% of total FA) exceeded the reference threshold (34.09-40.74% of FA) in both study groups: 55.240 [52.470; 56.185] % of FA and 45.900 [38.160; 50.290] % of FA, respectively. The subintimal inflammatory response risk index exhibited an increase both in the obesity group and in the control group (even higher in the latter): 57.090 [49.290; 82.385] % of FA and 136.990 [63.120; 210.860] % of FA, respectively). The polyunsaturated/saturated FA index showed levels of 0.400 [0.390; 0.485] % of FA and 0.810 [0.630; 1.160] % of FA in the main and control groups, respectively.
Conclusion — All the indices examined in children (whole blood ω-3 index, erythrocyte membrane ω-3 index, subintimal inflammatory response risk index, cell membrane viscosity, fluidity and permeability index) exhibited statistically significant changes in groups of obese adolescents. These changes were associated not only with increased cardiovascular risk and progression of chronic inflammation, but also with the nature of children's growth and development.

Keywords: obesity, fatty acids, lipidome, erythrocyte membrane indices, adolescents.

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Introduction

In recent years, increasing attention has been paid to the identification and study of early clinical markers of overweight and obesity, as shown by a literature review [1, 2].

From this standpoint, lipids, both endogenous and dietary, are of particular interest, probably playing a decisive role in the prevention and treatment of obesity [3].

It is known that fat accumulation is associated with the quality and quantity of fatty acids (FA) from the diet, and also adipose tissue secretes a wide range of substances that affect the development of obesity and related pathologies. Therefore, lipidomics can play a key role in describing molecular signaling scenarios, providing important information on the various stages of weight gain, from overweight to obesity [4, 5].

Lipidomics allows the identification of various types of lipids present in cells, tissues, biological fluids or throughout the body, reflecting lipid metabolism, including the early phase of pathophysiological changes associated with the development of the obesity phenotype. FA analysis, including membrane analysis, has reached a high level of technological maturity. Simple,

relatively inexpensive and robust analytical methods with high resolution have been developed and demonstrated in several studies [2, 6].

Various compartments can be used to assess the lipid composition of blood. FA in plasma or serum are widely analyzed, reflecting short-term changes associated with fat intake. In this regard, the analysis of the lipid composition of mature red blood cell membranes has an advantage over plasma analysis, since it maintains a more stable FA composition and better reflects the long-term effects of FA due to a longer circulation in the blood [2, 7].

Membrane lipids determine the qualitative characteristics of the lipid bilayer (fluidity, permeability, thickness) and its lipid signaling through the FA residues of membrane phospholipids. This suggests that FA may describe the predisposition of cells to respond to various stimuli from the extracellular environment [2, 8]. Thus, the balance of FA composition of membranes can affect the balance of functions in each individual cell and, consequently, in tissues and in the entire body [9, 10].

The goal of this study was to investigate the characteristics of the mobile pool of FA (including membrane indices) in adolescents with different body weights. This direction is of particular interest for a deeper understanding of the mechanisms of obesity phenotype formation in adolescents.

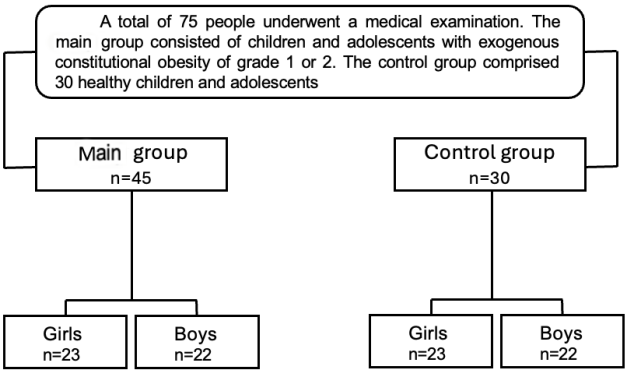

Figure 1. Flow chart illustrating the distribution of study participants among groups and subgroups.

Table 1. Main anthropometric parameters in groups of children with obesity and normal BMI (%, Me [Q1; Q3])

Parameter	*Main group (n=45)*	*Control group (n=30)*	*p*
Gender:			
male	22 (48.9%)	14 (46.7%)	1.000
female	23 (51.1%)	16 (53.3%)	
Age, years	14.7 [11.3; 16.2]	15.1 [11.8; 16.5]	0.623
Body mass, kg	79.7 [64.6; 94.5]	55.4 [51.8; 57.8]	<0.001
Height, m	162.0 [153.3; 172.5]	161.0 [155.0; 166.5]	0.871
BMI SDS	2.5 [2.1; 2.9]	0.3 [-0.4; 0.6]	<0.001

BMI SDS, body mass index standard deviation score; Me, median; Q1 and Q3, lower and upper quartiles; p, statistical significance of differences between groups (Mann-Whitney U test). *differences are significant at p<0.05.

Material and Methods

Study subjects

A single-center comparative study was conducted in parallel groups from September 2023 to February 2024 at the Children's Clinic (Director: MD D.V. Kozyritskaya) of the Siberian State Medical University of the Russian Federation Ministry of Healthcare, where overweight and obese children were examined and treated. Healthy schoolchildren of the Municipal Educational Institution, *Perspektiva School*, in Tomsk (Principal: I.E. Sakharova) were invited to participate in the study.

A total of 75 individuals were examined. The main group (n=45) comprised children and adolescents, including 22 boys (48.9%) and 23 girls (51.1%); their median age was 14.7 [11.3; 16.2] years with Grade 1 or 2 exogenous constitutional obesity. The control group consisted of 30 healthy children and adolescents, including 14 boys (46.7%) and 16 girls (53.3%), their median age was 15.1 [11.8; 16.5] years. The control and main groups were divided into subgroups based on gender (*Figure* 1).

The inclusion criteria for the main group were as follows: children and adolescents aged 10 to 17 years Grade 1 or 2 exogenous constitutional obesity (standard deviation score, SDS<3.0; body mass index, BMI≥2.0) who signed informed consent to participate in the study (approval by the Ethics Committee of Siberian State Medical University No. 8459/2 of October 28, 2020).

We employed the following exclusion criteria:

1. Monogenic obesity
2. Type 1 and Type 2 diabetes mellitus
3. Severe or unstable somatic diseases
4. Traumatic brain injury in anamnesis
5. History of alcoholism or drug addiction

Anthropometric measurements

Anthropometric assessment included height measurement to the nearest 0.1 cm, body weight to the nearest 0.1 kg without shoes and outerwear on the scale integrated into the InBody 770 analyzer (InBody Co., Ltd, Republic of Korea). The body mass index standard deviation score (BMI SDS) and SDS of height were calculated using the software developed by the World Health Organization (WHO): WHO AnthroPlus (for children aged 6 to 19 years) (URL: www.who-anthroplus.informer.com).

Analyzing mobile pool of fatty acids (lipoproteins and free fatty acids)

The mobile pool of FA (lipoproteins and free fatty acids, FFA) in serum was analyzed on an Agilent 7000B chromatograph mass spectrometer (Agilent Technologies, USA). The sample volume was 2 µl, injected with a split ratio of 1:5.

The range of specific parameters for the pool of FA included their following groups:

- Saturated fatty acids (SFA) with decanoic (10:0), lauric (12:0), myristoleic (14:0), palmitic (16:0), stearic (18:0), arachidic (20:0), behenic (22:0), and lignoceric (24:0) FA;
- Monounsaturated fatty acids (MUFA) with omega-5, 7 and 9 (ω-5, ω-7, ω-9): myristoleic (14:1n5), palmitoleic (16:1n7), oleic (18:1n9), erucic (22:1n9), nervonic (24:1n9), and eicosatrienoic FA (Mead acid) (20:3n9);

- Polyunsaturated fatty acids (PUFA) with omega-3 and 6 (ω-3, ω-6): linolenic (ALA 18:3n3), docosapentaenoic (DPA 22:5n3), docosahexaenoic (DHA 22:6n3), linoleic (LA 18:2n6), gamma-linolenic (GLA 18:3n6), dihomo-gamma-linolenic (DGLA 20:3n6), arachidonic (AA 20:4n6), and docosatetraenoic FA (adrenic acid) (DTA 22:4n6);
- Trans fatty acids (TFA): elaidic (ELA 18:1n9t) and linolelaidic FA;
- Odd-chain MUFA and SFA: pentadecanoic (15:0), margaric (heptadecanoic) (17:0), heneicosylic (21:0), tricosylic (23:0), and heptadecenoic (17:1n7).
- Multi-methyl-branched fatty acids: phytanic (3,7,11,15-tetramethylhexadecanoic) acid.

Additionally, we determined the relative content of FA in the groups and calculated the following indices and ratios: ω-3 FA and ω-6 FA in % of SFA; PUFA, MUFA, SFA, TFA in % of the total amount of FA; whole blood ω-3 index, erythrocyte membrane ω-3 index, ω-6/ω-3 FA ratio, and ω-6 desaturase activity index.

Statistical analyses were performed using IBM SPSS Statistics v.20 software. Frequency analysis was employed for qualitative data, and the results were presented as counts and percentages. Nominal data comparisons between groups were conducted using the Pearson's chi-squared test. In cases where the expected frequency in any cell of the 4-row/4-column table was less than 10, Fisher's exact test was used to assess the significance of differences.

Table 2. Detailed assessment of membrane and mobile (lipoprotein and free fatty acid) pools of fatty acids (FA) in whole blood in boys from both study groups (Me [Q1; Q3])

	Parameter	*% of FA*		*p*
		Main group (n=22)	Control group (n=14)	
ω -3 PUFA	Alfa-Linolenic (ALA 18:3n3)	0.250 [0.230; 0.278]	0.220 [0.160; 0.230]	0.011*
	Eicosapentaenoic (EPA 20:5n3)	0.08 [0.070; 0.100]	0.100 [0.040; 0.170]	0.797
	Docosapentaenoic (DPA 22:5n3)	0.240 [0.213; 0.280]	0.340 [0.340; 0.430]	0.043*
	Docosahexaenoic (DHA 22:6n3)	1.010 [0.880; 1.223]	2.100 [1.480; 2.210]	0.035*
ω -6 PUFA	Linoleic (LA 18:2n6)	16.360 [15.430; 19.485]	21.200 [18.810; 26.390]	0.637
	Gamma-linolenic (GLA 18:3n6)	0.110 [0.070; 0.148]	0.120 [0.110; 0.220]	0.164
	Dihomo-gamma-linolenic (DGLA 20:3n6)	0.760 [0.503; 0.860]	1.030 [0.820; 1.150]	0.004*
	Arachidonic (AA 20:4n6)	3.795 [3.428; 4.987]	7.870 [7.310; 8.550]	0.000*
ω -5 MUFA	Myristoleic (MOA 14:1n5)	0.040 [0.030; 0.95]	0.100 [0.050; 0.100]	0.020*
ω -7 MUFA	Docosatetraenoic (adrenic) (DTA 22:4n6)	0.340 [0.260; 0.545]	1.560 [0.830; 1.560]	<0.001*
	Palmitoleic (POA 16:1n7)	1.240 [1.073; 1.540]	0.860 [0.830; 0.870]	0.001*
ω -9 MUFA	Oleic (OA 18:1n9)	18.125 [16.470; 18.855]	13.870 [13.680; 13.870]	<0.001*
	Nervonic (NA 24:1n9)	1.895 [1.750; 2.050]	1.810 [1.790; 2.280]	0.716
	Eicosatrienoic (20:3n9, Mead's acid)	0.040 [0.030; 0.050]	0.040 [0.040; 0.070]	0.332
Saturated FA	Decanoic (DA 10:0)	0.020 [0.010; 0.020]	0.010 [0.010; 0.020]	0.169
	Lauric (LaA 12:0)	0.050 [0.013; 0.050]	0.020 [0.010; 0.050]	0.815
	Myristic (MA 14:0)	0.630 [0.490; 0.780]	0.230 [0.230; 0.480]	0.166
	Palmitic (PA 16:0)	32.260 [28.268; 32.870]	25.922 [22.460; 29.010]	0.001*
	Stearic (SA 18:0)	16.405 [15.025; 17.520]	15.250 [13.610; 15.250]	0.002*
	Arachidic (ANA 20:0)	0.375 [0.350; 0.400]	0.370 [0.320; 0.370]	0.053
	Behenic (BA 22:0)	1.410 [1.300; 1.520]	1.320 [1.270; 1.360]	0.015*
	Lignoceric (LCA 24:0)	2.550 [2.370; 2.900]	2.550 [2.140; 2.690]	0.183
	Phytanic	0.035 [0.020; 0.058]	0.060 [0.020; 0.090]	0.051
dd-chain MUFA and SFA	Heptadecanoic (GDA 17:1n7)	0.080 [0.070; 0.105]	0.080 [0.060; 0.080]	0.107
	Pentadecanoic (PDA 15:0)	0.275 [0.208; 0.305]	0.240 [0.180; 0.340]	0.955
	Margaric (MAA17:0)	0.370 [0.320; 0.438]	0.380 [0.240; 0.380]	0.131
	Heneicosylic (GEA 21:0)	0.010 [0.010; 0.018]	0.02 [0.010; 0.020]	0.409
	Tricosylic (TA 23:0)	0.310 [0.250; 0.430]	0.220 [0.210; 0.320]	0.024*
TFA	Elaidic (ELA 18:1n9t)	0.055 [0.033; 0.070]	0.030 [0.030; 0.040]	0.003*
	Linolelaidic (LELA 18:2ct)	0.080 [0.050; 0.173]	0.140 [0.060; 0.140]	0.875
Ratios	ω-3 FA (% of saturated FA)	1.595 [1.450; 1.835]	2.650 [2.300; 2.870]	0.001*
	ω-6 FA (% of saturated FA)	20.660 [19.610; 26.243]	30.320 [28.290; 37.980]	<0.001*
	Polyunsaturated FA, % of total FA	22.035 [21.070; 28.013]	33.200 [30.290; 40.630]	<0.001*
Ratios	Monounsaturated FA, % of total FA	21.515 [19.800; 22.715]	17.770 [16.820; 17.770]	<0.001*
	Saturated FA, % of total FA	54.210 [51.610; 56.333]	46.460 [42.520; 49.280]	<0.001*
	TFA, % of total FA	0.150 [0.105; 0.210]	0.170 [1.100; 0.170]	0.306
Calculated indices and ratios	ω-3 index for whole body (for a total of FFA, LP and CM)	1.335 [1.230; 1.540]	2.500 [2.080; 2.650]	<0.001*
	Erythrocyte membrane ω-3 index	1.620 [1.520; 1.813]	2.730 [2.330; 2.870]	<0.001*
	AA/EPA:(%AA/%EPA) Subintimal inflammatory response risk index**	51.320 [38.368; 57.260]	81.450 [63.120; 210.860]	0.025*
	ω-6/ω-3 FA index	13.310 [11.400; 16.705]	11.570 [10.560; 14.000]	0.059
	Polyunsaturated/saturated FA***	0.400 [0.375; 0.558]	0.740 [0.630; 0.990]	0.001*
	LA/DGLA. ω-6 desaturase activity index****	26.895 [20.125; 32.095]	18.490 [18.210; 29.900]	0.165

Me, median; Q1 and Q3, lower and upper quartiles; p, statistical significance of differences between groups (Mann-Whitney U test). *differences are significant at p<0.05; FA, fatty acids; FFA, free fatty acids; TFA, trans fatty acids; LP, lipoproteins; CM, cell membrane; ** subintimal inflammatory response risk index (risk of complications of cardiovascular diseases / level of the body's protective reserve; *** cell membrane viscosity, fluidity and permeability index; **** ω-6 desaturase activity index (efficiency of endogenous ω-6 FA formation).

Table 3. Detailed assessment of membrane and mobile (lipoproteins and free fatty acid) pools of fatty acids (FA) in whole blood in girls of both study groups (Me [Q1; Q3])

	Parameter	*% of FA*		*p*
		Main group (n=23)	Control group (n=16)	
ω-3 PUFA	Alfa-Linolenic (ALA 18:3n3)	0.260 [0.210; 0.275]	0.190 [0.124; 0.290]	0.071
	Eicosapentaenoic (EPA 20:5n3)	0.080 [0.060; 0.080]	0.105 [0.030; 0.170]	0.459
	Docosapentaenoic (DPA 22:5n3)	0.220 [0.210; 0.245]	0.395 [0.330; 0.990]	0.009*
	Docosahexaenoic (DHA 22:6n3)	1.070 [0.880; 1.275]	1.790 [0.330; 2.740]	0.140
ω-6 PUFA	Linoleic (LA 18:2n6)	16.500 [14.540; 17.510]	22.600 [1.580; 26.390]	0.713
	Gamma-linolenic (GLA 18:3n6)	0.140 [0.090; 0.180]	0.180 [0.140; 20.780]	0.080
	Dihomo-gamma-linolenic (DGLA 20:3n6)	0.710 [0.670; 0.880]	0.925 [0.700; 1.790]	0.038*
	Arachidonic (AA 20:4n6)	3.880 [3.800; 4.470]	7.930 [7.310; 10.440]	0.000*
ω-5 MUFA	Myristoleic (MOA 14:1n5)	0.080 [0.050; 0.100]	0.070 [0.050; 0.110]	0.783
ω-7 MUFA	Docosatetraenoic (adrenic) (DTA 22:4n6)	0.440 [0.230; 0.590]	1.155 [0.830; 1.480]	0.003*
	Palmitoleic (POA 16:1n7)	1.190 [0.975; 1.480]	0.850 [0.830; 0.870]	0.005*
ω-9 MUFA	Oleic (OA 18:1n9)	17.780 [15.980; 18.770]	13.690 [13.680; 13.700]	0.000*
	Nervonic (NA 24:1n9)	1.870 [1.765; 1.960]	1.810 [1.790; 2.100]	0.822
	Eicosatrienoic (20:3n9, Mead's acid)	0.040 [0.040; 0.050]	0.070 [0.050; 0.500]	0.069
Saturated FA	Decanoic (DA 10:0)	0.020 [0.015; 0.025]	0.015 [0.010; 0.020]	0.096
	Lauric (LaA 12:0)	0.050 [0.030; 0.110]	0.035 [0.020; 0.050]	0.904
	Myristic (MA 14:0)	0.820 [0.590; 1.110]	0.405 [0.330; 0.480]	0.077
	Palmitic (PA 16:0)	31.780 [29.245; 32.350]	25.735 [20.450; 29.010]	0.002*
	Stearic (SA 18:0)	16.630 [15.770; 17.690]	14.230 [13.280; 15.290]	0.000*
	Arachidic (ANA 20:0)	0.410 [0.400; 0.460]	0.335 [0.290; 0.400]	0.000*
	Behenic (BA 22:0)	1.420 [1.305; 1.530]	1.340 [1.080; 1.380]	0.015*
	Lignoceric (LCA 24:0)	2.630 [2.415; 2.990]	2.415 [1.970; 2.710]	0.026*
	Phytanic	0.060 [0.030; 0.065]	0.055 [0.020; 0.100]	0.853
Odd-chain MUFA and SFA	Heptadecanoic (GDA 17:1n7)	0.080 [0.070; 0.130]	0.065 [0.060; 0.080]	0.005*
	Pentadecanoic (PDA 15:0)	0.280 [0.250; 0.310]	0.260 [0.110; 0.340]	0.539
	Margaric (MAA17:0)	0.440 [0.400; 0.460]	0.275 [0.240; 0.420]	0.001*
	Heneicosylic (GEA 21:0)	0.020 [0.010; 0.035]	0.020 [0.010; 0.030]	0.377
	Tricosylic (TA 23:0)	0.350 [0.235; 0.430]	0.270 [0.170; 0.320]	0.068
TFA	Elaidic (ELA 18:1n9t)	0.050 [0.040; 0.065]	0.035 [0.030; 0.080]	0.213
	Linolelaidic (LELA 18:2ct)	0.100 [0.050; 0.235]	0.070 [0.020; 0.150]	0.075
Ratios	ω-3 FA (% of saturated FA)	1.680 [1.365; 1.910]	2.475 [2.060; 4.180]	0.003*
	ω-6 FA (% of saturated FA)	21.050 [19.130; 23.100]	33.135 [28.290; 38.770]	<0.001*
	Polyunsaturated FA, % of total FA	22.380 [20.790; 24.990]	35.460 [30.290; 42.950]	<0.001*
	Monounsaturated FA, % of total FA	21.160 [19.515; 22.585]	16.955 [16.820; 17.090]	<0.001*
	Saturated FA, % of total FA	55.240 [52.470; 56.185]	45.900 [38.160; 50.290]	<0.001*
	TFA, % of total FA	0.150 [0.120; 0.280]	0.100 [0.100; 0.180]	0.026*
Calculated indices and ratios	ω-3 index for whole body (for a total of FFA, LP and CM)	1.430 [1.130; 1.690]	2.290 [1.940; 3.900]	0.001*
	Erythrocyte membrane ω-3 index	1.710 [1.420; 1.960]	2.530 [2.190; 4.050]	0.001*
	AA/EPA:(%AA/%EPA) Subintimal inflammatory response risk index**	57.090 [49.290; 82.385]	136.990 [63.120; 210.860]	0.035*
	ω-6/ω-3 FA index	13.310 [11.430; 15.920]	12.785 [9.270; 14.000]	0.307
	Polyunsaturated/saturated FA***	0.400 [0.390; 0.485]	0.810 [0.630; 1.160]	0.001*
	LA/DGLA. ω-6 desaturase activity index****	22.610 [19.780; 24.550]	24.055 [14.730; 29.900]	0.977

Me, median; Q1 and Q3, lower and upper quartiles; p, statistical significance of differences between groups (Mann-Whitney U test). *differences are significant at p<0.05; FA, fatty acids; FFA, free fatty acids; TFA, trans fatty acids; LP, lipoproteins; CM, cell membrane; ** subintimal inflammatory response risk index (risk of complications of cardiovascular diseases / level of the body's protective reserve; *** cell membrane viscosity, fluidity and permeability index; **** ω-6 desaturase activity index (efficiency of endogenous ω-6 FA formation).

Statistical analyses were performed using IBM SPSS Statistics v.20 software. Frequency analysis was employed for qualitative data, and the results were presented as counts and percentages. Nominal data comparisons between groups were conducted using the Pearson's chi-squared test. In cases where the expected frequency in any cell of the 4-row/4-column table was less than 10, Fisher's exact test was used to assess the significance of differences.

Comparative and descriptive analysis of quantitative data was performed as well. For non-normally distributed quantitative data, medians and quartiles (Me [Q1; Q3]) were calculated. The normality of data distributions was tested using the Shapiro-Wilk test. Unpaired sample comparisons were performed using the Mann-Whitney U test.

Results

The main anthropometric characteristics of the groups are presented in *Table 1*. The control group did not differ significantly from the main group in age (p=0.623) and gender (p=1.000).

Regardless of gender, we observed statistically significant differences in lower levels of docosapentaenoic FA (ω-3 PUFA), dihomo-gamma-linolenic and arachidonic FA (ω-6 PUFA), docosatetraenoic (adrenic) FA (ω-7 MUFA) and, conversely, in higher levels of palmitoleic acid (ω-7 MUFA), oleic FA (ω-9 MUFA)

and representatives of SFA (palmitic, stearic, arachidic and behenic acids) in children with obesity vs. their peers with normal weight.

Comparison of the calculated indices demonstrated a statistically significant decrease in the relative content of ω-3, ω-6, PUFA, lower whole blood ω-3 index and erythrocyte membrane ω-3 index, lower PUFA/SFA ratio, and lower subintimal inflammatory response risk index [AA/EPA: (% AA/% EPA)] in children with obesity vs. those without excess weight. Detailed data are presented in *Tables* 2 and 3.

Boys

When comparing the FA pool indices that showed statistically significant differences in the groups of boys with laboratory reference ranges, we noted that in the ω-3 PUFA family, a reduced level of docosahexaenoic acid, 1.010 [0.880; 1.223] % of FA, was observed outside the reference range (1.42–5.43% of FA) in the group of children with obesity. Among the ω-6 PUFA, ω-5 MUFA and ω-9 MUFA families, the observed differences did not go beyond the reference ranges. However, for ω-7 MUFA, the level of docosatetraenoic acid, 0.340 [0.260; 0.545] % FA, was below the norm, which ranges 0.400–1.700 % of FA. Most of the SFA representatives (palmitic, stearic, arachidic and behenic acids) demonstrated an increase in their levels in the presence of obesity. However, in the control group, a similar trend was observed for stearic, arachidic and behenic acids.

When analyzing the ratios in the obese group: ω-3 FA (% of SFA) demonstrated a level of 1.595 [1.450; 1.835] % of FA; ω-6 FA (% of SFA) showed a decrease (20.660 [19.610; 26.243] % of FA) compared with the control data. SFA concentrations expressed as % of total FA exceeded the reference maximum in both the main and control groups: 54.210 [51.610; 56.333] % of FA and 46.460 [42.520; 49.280] % of FA, respectively. More details can be found in *Table* 4.

The whole blood ω-3 index of 1.335 [1.230; 1.540] % of FA and the erythrocyte membrane ω-3 index of 1.620 [1.520; 1.813] % of FA, when compared with the reference range, were interpreted as values corresponding to a high risk of cardiovascular diseases, since lower concentrations of ω-3 PUFA imply a shortage of anti-inflammatory mediators. The ω-6/ω-3 FA ratio in the presence of obesity (13.310 [11.400; 16.705] % of FA) exceeded the upper limit of the laboratory reference range (2.90-13.06% of FA), which predictably demonstrated an increased risk of proinflammatory responses.

Table 4. Comparison of the parameters of membrane and mobile (lipoproteins and free fatty acid) pools of fatty acids (FA) in whole blood of boys in the study groups (Me [Q1; Q3]) with reference laboratory values

	Parameter	*% of FA*		*Reference range*
		Grade 1 or 2 obesity, 2.0<BMI SDS<3.0 (n=45)	Normal body weight -1<BMI SDS<1 (n=26)	
ω-3 PUFA	Alfa-Linolenic (ALA 18:3n3)	0.250 [0.230; 0.278]	0.220 [0.160; 0.230]	0.12-0.66
	Docosapentaenoic (DPA 22:5n3)	0.240 [0.213; 0.280]	0.340 [0.340; 0.430]	0.50-1.52
	Docosahexaenoic (DHA 22:6n3)	1.010* [0.880; 1.223]	2.100 [1.480; 2.210]	1.42-5.43
ω-6 PUFA	Dihomo-gamma-linolenic (DGLA 20:3n6)	0.760 [0.503; 0.860]	1.030 [0.820; 1.150]	0.47-1.72
	Arachidonic (AA 20:4n6)	3.795 [3.428; 4.987]	7.870 [7.310; 8.550]	6.89-13.67
ω-5 MUFA	Myristoleic (MOA 14:1n5)	0.040 [0.030; 0.95]	0.100 [0.050; 0.100]	< 0.17
ω-7 MUFA	Docosatetraenoic (adrenic) (DTA 22:4n6)	0.340* [0.260; 0.545]	1.560 [0.830; 1.560]	0.400-1.700
	Palmitoleic (POA 16:1n7)	1.240 [1.073; 1.540]	0.860 [0.830; 0.870]	0.26-1.57
ω-9 MUFA	Oleic (OA 18:1n9)	18.125 [16.470; 18.855]	13.870 [13.680; 13.870]	12.68-19.66
Saturated FA	Palmitic (PA 16:0)	32.260* [28.268; 32.870]	25.922 [22.460; 29.010]	18.98-26.15
	Stearic (SA 18:0)	16.405* [15.025; 17.520]	15.250* [13.610; 15.250]	9.66-12.62
	Arachidic (ANA 20:0)	0.375* [0.350; 0.400]	0.370* [0.320; 0.370]	0.07-0.36
	Behenic (BA 22:0)	1.410* [1.300; 1.520]	1.320* [1.270; 1.360]	0.41-1.11
	Tricosylic (TA 23:0)	0.310 [0.250; 0.430]	0.220 [0.210; 0.320]	0.08-0.32
	Elaidic (ELA 18:1n9t)	0.055 [0.033; 0.070]	0.030 [0.030; 0.040]	-
Ratios	ω-3 FA (% of saturated FA)	1.595* [1.450; 1.835]	2.650 [2.300; 2.870]	2.25-9.61
	ω-6 FA (% of saturated FA)	20.660* [19.610; 26.243]	30.320 [28.290; 37.980]	31.16-42.48
	Polyunsaturated FA, % of total FA	22.035 [21.070; 28.013]	33.200 [30.290; 40.630]	36.67-47.73
	Monounsaturated FA, % of total FA	21.515 [19.800; 22.715]	17.770 [16.820; 17.770]	15.07-22.38
	Saturated FA, % of total FA	54.210* [51.610; 56.333]	46.460* [42.520; 49.280]	34.09-40.74
Calculated indices and ratios	ω-3 index for whole body (for a total of FFA, LP and CM)	1.335* [1.230; 1.540]	2.500 [2.080; 2.650]	2.1-4.3 – very high risk; 4.3-5.2 – high risk
	Erythrocyte membrane ω-3 index	1.620* [1.520; 1.813]	2.730* [2.330; 2.870]	<4 – high risk;
	AA/EPA:(%AA/%EPA) Subintimal inflammatory response risk index	51.320* [38.368; 57.260]	81.450* [63.120; 210.860]	>10 – high risk/extremely suboptimal protective reserve
	ω-6/ω-3 FA index	13.310* [11.400; 16.705]	11.570 [10.560; 14.000]	2.90-13.06
	Polyunsaturated/saturated FA	0.400* [0.375; 0.558]	0.740* [0.630; 0.990]	0-0.7 – significantly increased CM viscosity, reduced fluidity, and permeability 0.7-0.9 – moderately increased CM viscosity, reduced fluidity, and permeability

BMI SDS, body mass index standard deviation score; FA, fatty acids; FFA, free fatty acids; LP, lipoproteins; CM, cell membrane; Me, median; Q1 and Q3, lower and upper quartiles; * parameter values outside the laboratory reference range.

Table 5. Comparison of the parameters of membrane and mobile (lipoproteins and free fatty acid) pools of fatty acids (FA) in whole blood of girls in the study groups (Me [Q1; Q3]) with reference laboratory values

	Parameter	*% of FA*		*Reference range*
		Grade 1 or 2 obesity, 2.0<BMI SDS<3.0 (n=56)	Normal body weight -1<BMI SDS<1 (n=28)	
ω-3 PUFA	Docosapentaenoic (DPA 22:5n3)	0.220 [0.210; 0.245]	0.395 [0.330; 0.990]	0.50-1.52
ω-6 PUFA	Dihomo-gamma-linolenic (DGLA 20:3n6)	0.710 [0.670; 0.880]	0.925 [0.700; 1.790]	0.47-1.72
	Arachidonic (AA 20:4n6)	3.880* [3.800; 4.470]	7.930 [7.310; 10.440]	6.89-13.67
ω-7 MUFA	Docosatetraenoic (adrenic) (DTA 22:4n6)	0.440 [0.230; 0.590]	1.155 [0.830; 1.480]	0.400-1.700
	Palmitoleic (POA 16:1n7)	1.190 [0.975; 1.480]	0.850 [0.830; 0.870]	0.400-1.700
ω-9 MUFA	Oleic (OA 18:1n9)	17.780 [15.980; 18.770]	13.690 [13.680; 13.700]	12.68-19.66
Saturated FAs	Palmitic (PA 16:0)	31.780* [29.245; 32.350]	25.735 [20.450; 29.010]	18.98-26.15
	Stearic (SA 18:0)	16.630* [15.770; 17.690]	14.230* [13.280; 15.290]	9.66-12.62
	Arachidic (ANA 20:0)	0.410* [0.400; 0.460]	0.335 [0.290; 0.400]	0.07-0.36
	Behenic (BA 22:0)	1.420* [1.305; 1.530]	1.340* [1.080; 1.380]	0.41-1.11
	Lignoceric (LCA 24:0)	2.630* [2.415; 2.990]	2.415* [1.970; 2.710]	0.89-1.94
Odd-chain MUFA and SFA odd number of carbon atoms:	Heptadecenoic (GDA 17:1n7)	0.080 [0.070; 0.130]	0.065 [0.060; 0.080]	< 0.31
	Margaric (MAA17:0)	0.440* [0.400; 0.460]	0.275 [0.240; 0.420]	0.19-0.42
Ratios	ω-3 FA (% of saturated FA)	1.680* [1.365; 1.910]	2.475 [2.060; 4.180]	2.25-9.61
	ω-6 FA (% of saturated FA)	21.050* [19.130; 23.100]	33.135 [28.290; 38.770]	31.16-42.48
	Polyunsaturated FA, % of total FA	22.380* [20.790; 24.990]	35.460 [30.290; 42.950]	36.67-47.73
	Monounsaturated FAs, % of total FA	21.160 [19.515; 22.585]	16.955 [16.820; 17.090]	15.07-22.38
	Saturated FA, % of total FA	55.240* [52.470; 56.185]	45.900* [38.160; 50.290]	34.09-40.74
	TFA, % of total FA	0.150 [0.120; 0.280]	0.100 [0.100; 0.180]	<1 – recommended level; 1-1,65 – moderate (acceptable)
Calculated indices and ratios	ω-3 index for whole body (for a total of FFA, LP and CM)	1.430* [1.130; 1.690]	2.290 [1.940; 3.900]	2.1-4.3 – very high risk; 4.3-5.2 – high risk
	Erythrocyte membrane ω-3 index	1.710 [1.420; 1.960]	2.530 [2.190; 4.050]	<4 – high risk;
	AA/EPA:(%AA/%EPA) Subintimal inflammatory response risk index	57.090* [49.290; 82.385]	136.990* [63.120; 210.860]	>10 – high risk/extremely suboptimal protective reserve
	Polyunsaturated/ saturated FA (cell membrane viscosity, fluidity and permeability index)	0.400* [0.390; 0.485]	0.810* [0.630; 1.160]	0-0.7 – significantly increased CM viscosity, reduced fluidity, and permeability 0.7-0.9 – moderately increased CM viscosity, reduced fluidity, and permeability

BMI SDS, body mass index standard deviation score; FA, fatty acids; FFA, free fatty acids; TFA, trans fatty acids; LP, lipoproteins; CM, cell membrane; Me, median; Q1 and Q3, lower and upper quartiles. * parameter values outside the laboratory reference range.

The subintimal inflammatory response risk index was elevated in both groups, but it was significantly higher among adolescents with normal body weight: 51.320 [38.368; 57.260] % of FA and 81.450 [63.120; 210.860] % of FA, respectively. The PUFA/SFA ratio exhibited levels of 0.400 [0.375; 0.558] % of FA and 0.740 [0.630; 0.990] % of FA, respectively, in the main and control groups (see reference ranges in *Table 4*).

Girls

Analysis of the FA pool concentration, which yielded statistically significant differences in the groups of girls, when compared with laboratory reference ranges, revealed that the level of arachidonic acid representing the ω-6 PUFA family (3.880 [3.800; 4.470] % of FA) was statistically significantly lower in obesity group vs. the control group and fell below the lower limit of the reference range. Among the ω-9 MUFA, all FA, except oleic acid, exhibited an increase above the upper limit of the reference range in obesity. However, a similar trend was observed for stearic, behenic and lignoceric acids in individuals with normal weight. More details can be found in *Table 5*.

We noted that the levels of ω-3 FA (% of SFA) (1.680 [1.365; 1.910] % of FA) and ω-6 FA (% of SFA) (21.050 [19.130; 23.100] % of FA) were below the lower limit of the reference range. PUFA (% of total FA) were lower vs. the control and vs. reference values: 22.380 [20.790; 24.990] % of FA and 35.460 [30.290; 42.950] % of FA, respectively. SFA (% of total FA) exceeded the upper reference limit in both study groups: 55.240 [52.470; 56.185] % of FA and 45.900 [38.160; 50.290] % of FA, respectively (*Table 5*).

The subintimal inflammatory response risk index exhibited an increase in both the obesity group and control group (it was even higher in the latter): 57.090 [49.290; 82.385] % of FA and 136.990 [63.120; 210.860] % of FA, respectively). PUFA/SFA ratio showed levels of 0.400 [0.390; 0.485] % of FA and 0.810 [0.630; 1.160] % of FA, correspondingly, in the main and control groups.

Discussion

It is known that in adults, excess visceral fat is associated with changes in the composition of circulating FA and impaired adipose tissue function [11]. The opinion on the contribution of FA to the development of obesity, insulin resistance and other metabolic abnormalities in pediatric practice remains controversial.

The study by L.M. Beccarelli et al. (2018) showed that, regardless of obesity, changes in FA and lipid metabolism associated with the development of metabolic disorders can be observed. In contrast, the study by M.C. Hua et al. (2021) demonstrated that elevated palmitoleic acid levels were

associated with increased metabolic risk in obese and overweight children, as well as with the accumulation of visceral fat [13]. In this study, adolescents in the main group had statistically significantly higher levels of palmitoleic acid compared with the control group.

Similar results were obtained in the study by S. Bonafini et al. (2020) [14]. Dietary intake does not significantly affect the level of palmitoleic acid, which is formed as a result of palmitic acid metabolism by stearoyl-CoA desaturase-16 (SCD-16) [15]. In this study, palmitoleic acid levels and estimated SCD-16 activity were associated with obesity markers (BMI, waist-to-height ratio) and blood pressure, most pronounced in the obesity group. These results indicate that not only genetically determined increased SCD-16 activity but also other exogenous factors (including excessive palmitic acid intake) may support this association, leading to a metabolic response.

In addition, higher levels of arachidonic acid were noted in children with normal body weight, which contradicts the data on its adverse role in the development of insulin resistance. Several studies in both pediatric and adult populations demonstrated positive associations with insulin resistance and metabolic syndrome [2, 16, 17].

However, this study yielded reverse findings: non-obese adolescents had statistically significantly higher arachidonic FA levels. Similar results were obtained by S. Marth et al. (2020), who found an inverse relationship between arachidonic acid levels and HOMA-IR, with higher arachidonic acid levels in non-obese children [18]. The authors suggest that such conflicting data may be due to differences in the methods used and desaturase activity between the studied populations.

Both the main and control groups exhibited higher values of the subintimal inflammatory response risk index and the PUFA/SFA index vs. the control group. These parameters reflect the viscosity, fluidity, and permeability of the cell membrane. However, among adolescents with normal body weight, their levels were statistically significantly higher. These findings require further study, including dietary habits, which, according to publications, have a more substantial impact on the FA pool, including more steady red blood cell indices [2, 6].

In this study, obese adolescents had statistically significantly lower values of the whole blood ω-3 index and the erythrocyte membrane ω-3 index compared with the control group. Such results suggest an increased risk of cardiovascular disease.

Similar values of the erythrocyte membrane ω-3 index in studies involving adults were associated with a higher risk of coronary artery disease and were proposed as an addition to traditional scales (Framingham and GRACE) for predicting fatal cardiovascular events. They also correlated with the severity of insulin resistance [19, 20].

However, our obtained data cannot be extrapolated to the pediatric population, and changes in the FA profile associated with growth and development require further study. For example, I. Jauregibeitia et al. (2021) conducted a comparative analysis of erythrocyte FA indices in children and adults, demonstrating that obese children had higher levels of ω-6 PUFA (primarily, linoleic acid; $p<0.01$) and lower values of ω-3 FA (primarily, DHA; $p<0.001$) vs. adults [21].

The results of this study show significant changes in the mobile (lipoproteins and FFA) pool of FA in obese adolescents, suggesting that they are involved in the development of overweight and obesity and, therefore, can be considered as potential parameters for early clinical diagnosis.

Study limitations

Potential limitations of our study include the small sample size and data collection at a single center. Furthermore, adolescents with SDS BMI SDS>3 were excluded from the analysis, thereby making it difficult to compare the results with published data due to differences between cohorts. It is also important to note that the study did not assess dietary habits, which could have influenced the results.

Conclusion

All the indices examined in children (whole blood ω-3 index, erythrocyte membrane ω-3 index, subintimal inflammatory response risk index, cell membrane viscosity, fluidity and permeability index) exhibited statistically significant changes in the groups of adolescents with obesity. These changes were associated not only with increased cardiovascular risk, progression of chronic inflammation, but also with the nature of children's growth and development.

Conflict of interest

The authors declare no conflicts of interest.

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