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Physiological Rationale for Expanding the Spectrum of Traditional Lipid Metabolism Parameters in Indigenous Males of the Arctic Region

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ABSTRACT

BACKGROUND: Early physiological and biochemical studies reported relatively favorable lipid profiles in terms of protection against cardiovascular risk factors. However, in recent decades, a shift toward a more atherogenic lipid profile has been observed in some apparently healthy individuals living in the North. An expanded lipid panel includes the assessment of apolipoproteins and free fatty acids. There is a growing need for in-depth investigation of lipid metabolism in individuals without clinical signs of its disturbance residing in the Arctic zone to enable early diagnosis, timely correction, and prevention of cardiovascular diseases.

AIM: To substantiate the selection of a set of lipid metabolism alteration markers in apparently healthy indigenous males of the Arctic region.

MATERIALS AND METHODS: A total of 112 apparently healthy men permanently residing in the Arkhangelsk Region were examined. Serum levels of total cholesterol, high-, low-, and very-low-density lipoproteins, triglycerides, atherogenic index, concentrations of saturated, monounsaturated, and polyunsaturated fatty acids, as well as the apolipoprotein A to B ratio were determined.

RESULTS: It was found that, although the levels of total cholesterol, high-, low-, and very-low-density lipoproteins, triglycerides, and the atherogenic index did not exceed reference values in apparently healthy residents of the Arctic region, elevated levels of very-low-density lipoproteins (19.8% of participants), triglycerides (17.2%), and the atherogenic index (52.1%) were observed. Apolipoprotein A levels were below reference values but exceeded apolipoprotein B levels in 39.1% of cases; the apolipoprotein A to B ratio was elevated in 51.2% of subjects. High levels of the palmitic (12.5%) and stearic (10.7%) saturated fatty acids were observed. In contrast, levels of polyunsaturated fatty acids were below the median in the case of ω-6 linoleic (21.4%) and arachidonic (51.5%) acids, as well as ω-3 alpha-linolenic (51.8%), eicosapentaenoic (40.8%), and docosahexaenoic (48.3%) acids. Moderate correlations were identified between triglyceride levels and saturated fatty acids, as well as weaker correlations with polyunsaturated fatty acids.

CONCLUSION: Markers of subclinical lipid metabolism disturbances in indigenous residents of the Arctic region include relatively low levels of apolipoprotein A, a higher apolipoprotein B to A ratio, and reduced concentrations of ω-3 (alpha-linolenic, eicosapentaenoic, docosahexaenoic) and ω-6 (linoleic, arachidonic) polyunsaturated fatty acids.

Keywords: lipid metabolism; apolipoproteins; free fatty acids; Russian Arctic region.

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Физиологическое обоснование расширения исследования спектра традиционных параметров липидного обмена у коренного мужского населения Арктического региона

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АННОТАЦИЯ

Обоснование. В ранних физиолого-биохимических исследованиях представлены данные об относительно благоприятных профилях липидного обмена в отношении протекции факторам риска развития патологии сердечно-сосудистой системы. Однако в последние десятилетия у части практически здоровых северян стали выявляться изменения липидного профиля крови атерогенной направленности. Расширенный спектр параметров липидного обмена включает изучение аполипопротеинов и свободных жирных кислот. Возникает необходимость углублённого изучения липидного обмена у лиц без клинических признаков его нарушений, проживающих в Арктической зоне, для ранней диагностики, коррекции и профилактики патологии сердечно-сосудистой системы.

Цель. Обоснование выделения совокупности маркеров изменения липидного обмена у практически здорового коренного мужского населения Арктического региона.

Материалы и методы. Проведено обследование 112 практически здоровых мужчин, постоянно проживающих в Архангельской области. В сыворотке крови определяли содержание общего холестерина, липопротеинов высокой, низкой и очень низкой плотности, триглицеридов, коэффициент атерогенности, концентрацию насыщенных, мононенасыщенных и полиненасыщенных жирных кислот, соотношение аполипопротеинов А и В.

Результаты. Установлено, что при невыходящем за пределы референсных значений содержании общего холестерина, липопротеинов высокой, низкой и очень низкой плотности, триглицеридов, коэффициента атерогенности у практически здоровых жителей Арктического региона имеется высокое содержание липопротеинов очень низкой плотности (19,8% обследуемых), триглицеридов (17,2%), коэффициента атерогенности (52,1%); содержание аполипопротеинов А ниже референсных значений, но выше аполипопротеинов В (39,1%), соотношение аполипопротеинов А и В было высоким (51,2 %). Отмечается высокое содержание пальмитиновой (12,5%), стеариновой (10,7%) насыщенных жирных кислот. Напротив, значения ниже медианы отмечены в содержании ω-6 линолевой (21,4%), арахидоновой (51,5%), ω-3 линоленовой (51,8%), эйкозопентаеновой (40,8%), докозагексаеновой (48,3%) полиненасыщенных жирных кислот. Установлены взаимосвязи средней силы между триглицеридами и насыщенными жирными кислотами, но более слабые с полиненасыщенными жирными кислотами.

Заключение. Маркерами скрытых нарушений липидного обмена у жителей Арктического региона являются относительно низкое содержание аполипопротеинов А, но более высокое соотношение аполипопротеинов В и А, а также низкое содержание ω-3 линоленовой, эйкозопентаеновой, докозагексаеновой и ω-6 линолевой, арахидоновой полиненасыщенных жирных кислот.

Ключевые слова: липидный обмен; аполипопротеины; свободные жирные кислоты; Арктический регион России.

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北极地区原住男性脂质代谢传统参数谱扩展研究的生理学依据

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摘要

论证。早期的生理-生化研究提供了有关脂质代谢相对有利特征的数据，这些特征与对心血管疾病风险因素的保护作用相关。然而，近几十年来，部分临床健康的北方居民已被发现存在动脉粥样硬化倾向的血脂谱改变。脂质代谢参数谱的拓展应包括对载脂蛋白和游离脂肪酸的检测。因此，有必要对居住在北极地区、无临床脂质代谢紊乱表现的人群进行深入研究，以实现心血管系统疾病的早期诊断、干预和预防。

目的。论证在北极地区临床健康的原住男性人群中划定脂质代谢变化标志物组合的合理性。

材料与方法。研究对象为112名常住Arkhangelsk州、临床表现健康的男性。检测其血清中的总胆固醇、高密度、低密度和极低密度脂蛋白、甘油三酯、动脉粥样硬化指数，以及饱和、单不饱和和多不饱和脂肪酸的含量，并评估载脂蛋白A与B的比值。

结果。在大多数总胆固醇、高密度、低密度及极低密度脂蛋白、甘油三酯和动脉粥样硬化指数等指标未超出参考范围的背景下，部分北极地区临床健康受试者仍表现出极低密度脂蛋白偏高（19.8%）、甘油三酯偏高（17.2%）、动脉粥样硬化指数升高（52.1%）；载脂蛋白A 水平低于参考值，而载脂蛋白B 水平较高（39.1%），A/B 比值较高（51.2%）。此外，棕榈酸（12.5%）和硬脂酸（10.7%）等饱和脂肪酸水平较高。而ω-6亚油酸（21.4%）、花生四烯酸（51.5%）、ω-3亚麻酸（51.8%）、二十碳五烯酸（40.8%）、二十二碳六烯酸（48.3%）等多不饱和脂肪酸水平则普遍偏低。甘油三酯与饱和脂肪酸呈中等强度相关，与多不饱和脂肪酸的相关性相对较弱。

结论。北极地区居民潜在脂质代谢异常的标志物包括：载脂蛋白A含量相对较低、载脂蛋白B与A的比值较高，以及ω-3系列（α-亚麻酸、二十碳五烯酸、二十二碳六烯酸）和ω-6系列（亚油酸、花生四烯酸）多不饱和脂肪酸含量较低。

关键词：脂质代谢；载脂蛋白；游离脂肪酸；俄罗斯北极地区。

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BACKGROUND

Early physiological and biochemical studies reported distinctive features of metabolic processes among residents in Arctic regions, determined by a biologically established adaptive type and associated with a traditional lifestyle and a diet rich in fats and proteins [1]. Indigenous populations, characterized by the northern type of metabolism, demonstrated more favorable lipid profiles that appear to confer protection against cardiovascular risk factors. Lower serum levels of total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL), and very-low-density lipoprotein (VLDL), along with higher levels of high-density lipoprotein (HDL), have been observed compared with nonindigenous populations [2]. The current approach to assessing cardiovascular status includes the identification of risk factors and clinical symptoms of atherosclerosis, measurement of blood lipid profile, and evaluation of cardiovascular risk using the SCORE scale. Lipid profile parameters used to assess cardiovascular risk include TC, HDL, LDL, and TG. However, the analysis of these parameters does not always allow for a targeted evaluation of existing disturbances, especially given the growing emphasis on early detection of biochemical abnormalities in metabolic processes rather than on the identification of clinical manifestations [3].

In recent years, metabolic disorders have become increasingly common among residents of the Arctic regions. Primary contributing factors include physical inactivity and poor dietary habits [4], accompanied by a gradual decline in the consumption of traditional foods (e.g., reindeer meat, fish from northern seas) and increased intake of carbohydrates and trans fats [5].

There is an increasing number of studies that focus on an extended range of lipid metabolism parameters, including apolipoproteins and free fatty acids (FFAs). Currently, apolipoproteins B and A1 (ApoB and ApoA1) are considered the most reliable markers of lipid profile abnormalities. ApoB (specifically ApoB-100) is a structural component of VLDL, intermediate-density lipoproteins, and LDL, with each lipoprotein particle containing only one apolipoprotein molecule. Therefore, the ApoB level reflects the total number of atherogenic particles in the bloodstream. In contrast, ApoA1 is a structural component of antiatherogenic HDL. Thus, the ApoB/ApoA1 ratio reflects the balance between atherogenic and antiatherogenic lipoproteins and serves as an early potential marker of cardiovascular disease risk [6].

Apolipoproteins contain ligands that bind to membrane receptors, enabling the entry of lipoproteins into cells and their subsequent catabolism. They also serve as cofactors for enzymes that are needed for the proper functioning of lipoproteins. During lipoprotein formation in hepatocytes, apolipoproteins bind various TGs, depending on the types of fatty acids esterified with the hydroxyl groups of glycerol. This, in turn, influences the density of the TGs and the lipoproteins that contain them [7]. Most fatty acids are found in a bound form as components of phospholipids, TGs, and TC esters, and the specific type of fatty acid significantly affects many of their properties.

The ratio of consumed fatty acids plays a significant role in determining the composition of TGs, particularly in relation to an increase in saturated fatty acids (SFAs) and a decrease in polyunsaturated fatty acids (PUFAs). Fatty acids can affect lipoprotein proteins by destabilizing them, thereby impairing their functionality and rendering them dysfunctional. Alterations in the proteome and/or lipidome of HDL result in HDL dysfunction, manifested by impaired antioxidant and anti-inflammatory functions [8]. An imbalance in the content of fatty acids, TGs, and lipoproteins may contribute to inflammation through the synthesis of inflammatory mediators. To better understand these mechanisms, it is particularly important to assess an extended lipid profile, including apolipoproteins and fatty acid composition.

Only a few clinical reports describe the combined analysis of traditional lipid profile parameters, apolipoproteins, SFAs, PUFAs, and FFAs [9]. However, no data are available on their combined changes in apparently healthy individuals living at high latitudes. This highlights the need for in-depth investigation of lipid metabolism in individuals without clinical signs of its disturbance residing in the Arctic zone to enable early diagnosis, timely correction, and prevention of cardiovascular diseases.

AIM. The work aimed to substantiate the selection of a set of lipid metabolism alteration markers in apparently healthy indigenous males of the Arctic region.

MATERIALS AND METHODS

This cross-sectional study included 112 apparently healthy men aged 22 to 55 years (mean age: 43.57 ± 1.43 years), all indigenous residents of Arkhangelsk. All participants completed questionnaires collecting information on age, anthropometric parameters, ethnicity (self-reported and parental), duration of residence in the North, medical history, dietary habits, and other relevant factors. The individuals with a history or clinical signs of alcohol or tobacco dependence or exposure to occupational hazards (including shift and night work) were excluded.

Primary blood lipid profile parameters were evaluated. Venous blood samples were collected from the cubital vein after an overnight fast (between 8:00 and 10:00 a.m.) using Becton Dickinson BP vacutainers.

Levels of TC, HDL, VLDL, LDL, and TGs were measured by turbidimetric analysis using a FURUNO CA-270 biochemical analyzer (Japan) and Chronolab AG reagent kits (Switzerland). VLDL was calculated as TG/5. The atherogenic coefficient (AC) was determined using Klimov's formula [10]: AC=(TC–HDL)/HDL. Concentrations of apolipoproteins (ApoA and ApoB) were measured by immunoturbidimetric assay using the FURUNO CA-270 biochemical analyzer (Japan) and Chronolab AG reagent kits (Switzerland). The ApoB/ApoA ratio was also calculated.

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The content of SFAs, monounsaturated fatty acids (MUFAs), and PUFAs, including ω-3 and ω-6 fatty acids, was determined by gas–liquid chromatography following preliminary lipid extraction from blood serum and subsequent methylation of fatty acids to obtain their methyl esters [11]. Methylated fatty acid derivatives were analyzed using an Agilent 7890A gas chromatograph (flame ionization detector; Agilent DB-23 capillary column, 60×0.25×0.15 mm) in programmed temperature mode with nitrogen as the carrier gas. Fatty acids were identified using standard mixes Supelco 37 FAME C_4–C_{24} (USA) and GLS-569B (Nu-Chek-Prep, Inc., USA). The quantification of fatty acids was performed using the internal standard method (nonadecanoic acid) with the Agilent ChemStation B.03.01 software (USA).

The study was conducted in accordance with the principles of the World Medical Association Declaration of Helsinki: ethical principles for medical research [12]. Written informed consent was provided by all participants. The study protocol was approved by the Ethics Committee of the Federal Research Center for Integrated Arctic Studies, Ural Branch of the Russian Academy of Sciences (Protocol No. 12, dated February 15, 2022).

The statistical analysis of the obtained data, including assessment of the distribution of variables and comparative analysis of samples, was performed using SPSS software, version 15.0. Quantitative variables were described using the median (MD), first quartile (Q25), and third quartile (Q75). The Shapiro–Wilk test was used to assess normality of distribution, which showed that most variables did not follow a normal distribution. Therefore, nonparametric tests were used. The correlation analysis was performed using Spearman rank correlation coefficient. The strength of correlation was considered strong for r >0.70, moderate for r=0.30–0.69, and weak for r <0.29.

RESULTS

No significant deviations in traditional lipid metabolism parameters from the reference values (as indicated in the instructions for the test kits used) were identified among apparently healthy individuals residing in the Arctic region. However, elevated levels of VLDL were found in 19.8% of participants, TGs in 17.2%, and the AC in 52.1% (Table 1).

Several studies have demonstrated that TC, which was previously considered a primary cardiovascular risk factor, is neither the only nor the principal factor [13]. This underscores the need for a more detailed analysis of the lipid profile to detect subclinical abnormalities and supports the evaluation of serum apolipoprotein and FFA levels.

In this context, a targeted assessment of apolipoproteins as potential markers of lipid metabolism disturbances was conducted. It was found that the mean ApoA level was below the reference range, ApoB levels were elevated in 39.1% of participants, and the ApoB/ApoA ratio was elevated in 51.2% (Table 2).

The analysis of the most clinically significant SFAs and MUFAs showed that the levels of palmitic acid (C16:0), stearic acid (C18:0), and oleic acid (C18:1ω9) generally remained within the reference range in the northern population. However, elevated levels of palmitic acid were observed in 12.5% of cases and elevated levels of stearic acid in 10.7% (Table 3).

The levels of PUFAs from the ω-3 and ω-6 families were assessed (Table 4). No reduction in the mean level of linoleic acid (C18:2ω6), a representative of ω-6 PUFAs, was observed; however, its concentration was below the median in 21.4% of cases. A low level of arachidonic acid (C20:4ω6), 15.2% below the reference values, was observed; values below the median were identified in 51.5% of participants.

The level of α-linolenic acid (C18:3ω3), a representative of ω-3 PUFAs, was within reference values, although values below the median were found in 51.8% of participants. The levels of eicosapentaenoic acid (C20:5ω3) and docosahexaenoic acid (C22:6ω3) did not differ significantly from the reference values; however, concentrations below the median were observed for eicosapentaenoic acid (C20:5ω3) and docosahexaenoic acid (C22:6ω3) in 40.8% and 48.3% of participants, respectively.

The relevance of assessing SFAs in apparently healthy individuals for identifying latent changes in lipid metabolism is supported by the detection of correlations between SFAs and traditional lipid profile parameters.

In individuals residing in the Arctic region, moderate correlations were found between TGs and SFAs, MUFAs, and weaker correlations with PUFAs, indicating the incorporation of fatty acids into TG and LDL. Specifically, correlations were found between TG and the SFAs: myristic acid (C14:0; r=0.649; p <0.0001), pentadecanoic acid (C15:0; r=0.469; p <0.001), palmitic acid (C16:0; r=0.581; p <0.001), margaric acid (C17:0; r=0.560; p <0.001), stearic acid (C18:0; r=0.551; p <0.001);

Table 1. Traditional lipid metabolism parameters in apparently healthy residents of the Arctic region

Parameters	Reference range	Values in apparently healthy individuals, Me (Q25; Q75)
Total cholesterol, mmol/L	2.99–6.09	4.74 (4.22; 5.62)
Very-low-density lipoproteins, mmol/L	0.16–0.46	0.28 (0.16; 0.46)
Low-density lipoproteins, mmol/L	3–7	4.24 (3.13; 5.95)
High-density lipoproteins, mmol/L	0.85–1.94	1.19 (0.98; 1.36)
Atherogenic index	up to 3.0	3.10 (2.07; 4.40)
Triglycerides, mmol/L	0.8–2.3	1.40 (0.82; 1.98)

MUFAs: myristoleic acid (C14:1; r=0.448; p <0.001), palmitoleic acid (C16:1; r=0.529; p <0.001), oleic acid (C18:1ω9; r=0.647; p <0.001); ω-6 PUFAs: linoleic acid (C18:2ω6; r=0.425; p <0.001), γ-linolenic acid (C18:3ω6; r=0.495; p <0.001), dihomo-γ-linolenic acid (C20:3ω6; r=0.348; p=0.001), arachidonic acid (C20:4ω6; r=0.208; p=0.042); ω-3 PUFAs: α-linolenic acid (C18:3ω3; r=0.484; p <0.001), eicosatrienoic acid (C20:3ω3; r=0.352; p=0.005), docosahexaenoic acid (C22:6ω3; r=0.245; p=0.005). Correlations were established between ω-6 PUFAs: linoleic acid (C18:2ω6) and γ-linolenic acid (C18:3ω6; r=0.724; p=0.001); γ-linolenic acid (C18:3ω6) and dihomo-γ-linolenic acid (C20:3ω6; r=0.470; p < 0.001); and dihomo-γ-linolenic acid (C20:3ω6) and arachidonic acid (C20:4ω6; r=0.726; p=0.001).

The main sources of long-chain ω-3 PUFAs (eicosapentaenoic acid and docosahexaenoic acid) are marine fish oils [14]. Partially, ω-3 PUFAs (eicosapentaenoic and docosahexaenoic) are formed from α-linolenic acid; this process proceeds as follows: α-linolenic acid → eicosatrienoic acid → eicosapentaenoic acid → docosahexaenoic acid.

Correlations were identified between α-linolenic acid (C18:3ω3) and eicosatrienoic acid (C20:3ω3; r=0.435; p=0.01); eicosapentaenoic acid (C20:5ω3; r=0.501; p <0.001) and docosahexaenoic acid (C22:6ω3; r=0.496; p=0.001). This chain lacks an intermediate link: the conversion of eicosatrienoic acid (C20:3ω3) to eicosapentaenoic acid (C20:5ω3; r=0.501; p <0.001).

DISCUSSION

No significant deviations from reference values were identified when evaluating the results of traditional lipid metabolism parameters in apparently healthy residents of the Arctic region. However, elevated levels of atherogenic VLDL fractions, TGs, and particularly the AC were observed in 52.1% of participants. The analysis of apolipoprotein levels revealed a low mean ApoA concentration, whereas elevated ApoB levels and an increased ApoB/ApoA ratio were identified in 39% to 51% of individuals.

A study by Pashinskaya et al. [15] reported a low serum ApoA level in a substantial proportion of apparently healthy individuals residing in the Far North. The ApoB/ApoA1 ratio reflects the balance between atherogenic ApoB and antiatherogenic ApoA1 particles and is considered one of the markers of cardiovascular risk [16].

The levels of TGs, LDLs, and HDLs are known to depend on the intake of SFAs in the diet. Dietary enrichment with PUFAs results in a reduction in LDL levels without significantly affecting antiatherogenic HDL concentrations. Several studies have shown that PUFA consumption is associated with reduced TG, TC, fibrinogen, and VLDL levels, as well as increased HDL concentrations [17].

Earlier studies by Boyko et al. [18] and Lyudinina et al. [19] demonstrated that among the indigenous population of the North, particularly those adhering to a traditional protein–lipid diet, there is an increased content of ω-3 PUFAs (eicosapentaenoic and docosahexaenoic acids), along with decreased levels of ω-6 PUFAs. Higher PUFA levels were observed in the residents of the Arctic regions compared with those living in southern regions [20].

The analysis of SFA, MUFA, and PUFA levels showed that the most significant SFAs involved in the composition of TG and LDL were palmitic acid (C16:0) and stearic acid (C18:0), along with the MUFA oleic acid (C18:1ω9). SFAs are a major source of energy for the body. It is well known that their levels depend on dietary patterns, which vary by region. SFAs

Table 2. Apolipoprotein levels in apparently healthy residents of the Arctic region

Parameters	Reference range	Values in apparently healthy individual. Me (Q25; Q75)
Apolipoprotein A, mg/dL	122–161	84.90 (76.08; 97.12)
Apolipoprotein B, mg/dL	69–105	90.49 (72.85; 120.42)
Apolipoprotein B to A ratio	up to 1.0	1.09 (0.93; 1.35)

Table 3. Levels of saturated and monounsaturated fatty acids in apparently healthy residents of the Arctic region, μg/ml

Fatty acids	Reference range	Values in apparently healthy individuals, Me (Q25; Q75)
C14:0 Myristic	5.70–28.00	15.92 (10.14; 27.48)
C15:0 Pentadecanoic	1.88–7.92	4.36 (3.27; 5.38)
C16:0 Palmitic	217.50–570.34	352.66 (284.65; 111.53)
C17:0 Margaric	2.88–9.17	4.92 (3.75; 6.51)
C18:0 Stearic	83.44–197.16	132.61 (112.66; 175.30)
C14:1 Myristoleic	0.11–2.16	1.06 (0.82; 1.57)
C15:1 Pentadecenoic	0.10–1.15	0.65 (0.29; 1.05)
C16:1 Palmitoleic	10.20–65.50	21.41 (14. 09; 39.10)
C18:1 ω9 Oleic	137.40–660.50	246.92 (195.56; 395.96)

Table 4. Levels of polyunsaturated fatty acids in apparently healthy residents of the Arctic region, μg/ml

Parameters	Reference range	Values in apparently healthy individuals, Me (Q25; Q75)
C18:2 ω6 Linoleic	201.50–1500.25	581.53 (369.82; 716.41)
C18:3 ω6 γ-Linolenic	0.23–25.50	4.13 (2.67; 5.65)
C20:3 ω6 Dihomo-γ-linolenic	3.53–33.86	13.47 (9.04; 20.26)
C20:4 ω6 Arachidonic	85.24–160.97	73.70 (42.22; 107.12)
C18:3 ω3 α-Linolenic	0.25–11.02	4.09 (2.11; 5.70)
C20:3 ω3 Eicosatrienoic	0.25–4.50	0.60 (0. 30; 1.32)
C20:5 ω3 Eicosapentaenoic	2.25–80.50	8.93 (3.81; 19.72)
C22:6 ω3 Docosahexaenoic	5.50–110.20	33.00 (11.94; 60.55)

are primarily found in animal fats. On the one hand, elevated SFA levels may be necessary to ensure energy reserves; on the other hand, their excessive intake can contribute to TG and LDL accumulation, thereby promoting the development of atherosclerotic changes. Evidence of latent disturbances in lipid metabolism is also supported by the finding that some of the individuals examined in the North had elevated SFA levels. This may, to some extent, be associated with changes in diet, including increased consumption of trans fats, fast food, and related products.

We also assessed the levels of ω-3 and ω-6 PUFAs. In 21.4% of cases, low levels of ω-6 linoleic acid were detected; the level of ω-6 arachidonic acid was below the median in 51.5% of participants. Low levels (below the median) of ω-3 PUFAs (α-linolenic, eicosapentaenoic, and docosahexaenoic acids) were observed in 40%–50% of the individuals.

ω-6 linoleic acid (C18:2ω6c) and ω-3 α-linolenic acid (C18:3ω3) are essential fatty acids. Some authors also consider arachidonic acid (C20:4ω6) essential. These fatty acids are present in vegetable oils, whereas small amounts of arachidonic acid are found in pork fat and dairy products.

The ω-3 family includes α-linolenic acid (C18:3ω3), eicosapentaenoic acid (C20:5ω3), and docosahexaenoic acid (C22:6ω3), which are primarily found in the fat of marine fish from northern seas. In cells and tissues, long-chain PUFAs are not present in free form but are incorporated into various lipid classes, including TGs, phospholipids, and cholesterol esters. Fatty acids constitute approximately 60% of the dry mass of the brain, with the highest concentrations found in neuronal membranes. In the gray matter of the cerebral cortex in healthy individuals, docosahexaenoic acid accounts for up to 13% and arachidonic acid up to 9% of total fatty acids; in the retina, approximately 60% of PUFAs are represented by docosahexaenoic acid. The composition of membrane phospholipids affects electrophysiological responsiveness, which explains the high content of arachidonic and docosahexaenoic acids in organs with intense electrophysiological activity, such as the brain, retina, and synapses [21].

To clarify the role of SFAs in lipid metabolism among residents of the Arctic region, a correlation analysis was performed. It revealed associations between TGs and SFAs, MUFAs, and PUFAs, which may indicate the incorporation of fatty acids into TGs. Correlations were also identified among ω-6 and ω-3 PUFAs: in particular, associations between linoleic acid and γ-linolenic, dihomo-γ-linolenic, and arachidonic acids were observed. These findings indicate that the conversion of linoleic acid to arachidonic acid is not impaired. Arachidonic acid is predominantly derived from dietary sources (animal fats); thus, its reduced levels are likely due to insufficient dietary intake. However, small amounts of arachidonic acid can also be synthesized from ω-6 linoleic acid via its intermediate conversion to γ-linolenic acid, then to dihomo-γ-linolenic acid, and subsequently to arachidonic acid.

We identified correlations between the ω-3 PUFA α-linolenic acid (C18:3ω3) and eicosatrienoic acid (C20:3ω3); however, no correlation was found between eicosatrienoic acid (C20:3ω3) and eicosapentaenoic acid (C20:5ω3). Only correlations between eicosapentaenoic acid (C20:5ω3) and docosahexaenoic acid (C22:6ω3) were observed. This may indicate a disruption in the conversion of eicosatrienoic acid (C20:3ω3) to eicosapentaenoic acid (C20:5ω3). The synthesis of both ω-6 and ω-3 PUFAs involves the same enzymes (elongase and desaturase), participating competitively in the synthesis of ω-6 and ω-3 PUFAs [22]. It is possible that these enzymes are preferentially utilized for ω-6 PUFA synthesis.

Undoubtedly, genetic factors also influence lipid metabolism, and these may differ among populations from various geographic regions. However, a unified viewpoint has not been established. For example, Bichkaeva et al. [23] compared blood lipid profiles in residents of the polar regions of the North and the southern Caucasus (South Ossetia). Residents of the North had higher levels of not only LDL and VLDL, but also HDL and ApoA. However, they also exhibited elevated ApoB levels and a higher ApoB/ApoA ratio compared with those residing in the southern Caucasus, indicating an imbalance in apolipoproteins. Krivoshapkina et al. [24] found no significant sex-based differences in lipid metabolism among residents of Yakutia. In a work by Shaimardanov and Litovchenko [25], the indigenous population of Yakutia showed a high prevalence of atherogenic dyslipidemia and obesity based on biochemical blood parameters. Our study did not aim to include indigenous residents of the Arctic

regions, as this would require a targeted and more detailed investigation. Therefore, the findings presented here should be interpreted with this limitation in mind.

CONCLUSION

This study demonstrated that apparently healthy residents of the Arctic region exhibit latent disturbances in lipid metabolism, as evidenced by elevated levels of VLDL, TGs, the AC, ApoB, and the ApoB/ApoA ratio, along with reduced ApoA levels in some residents. The decreased concentrations of ω-6 PUFAs, particularly linoleic and arachidonic acids, and ω-3 PUFAs (eicosapentaenoic and docosahexaenoic acids) may be due to both insufficient dietary intake and competition for enzymes involved in their metabolic conversion. To identify latent lipid metabolism disorders in apparently healthy individuals living in the Arctic region, it is important to assess both traditional lipid profile parameters and additional markers, including ApoA and ApoB, the ApoB/ApoA ratio, as well as levels of ω-3 (eicosapentaenoic and docosahexaenoic) and ω-6 (linoleic and arachidonic) PUFAs.

ADDITIONAL INFORMATION

Author contributions: N.V. Solovieva: conceptualization; V.A. Solovyeva, U.G. Guseynova: investigation; V.A. Solovyeva, F.A. Bichkaeva: clinical data collection and processing, database development; A.G. Soloviev: formal analysis, writing—review & editing. All authors confirm that their authorship meets the ICMJE criteria (all authors made substantial contributions to the conceptualization, investigation, and manuscript preparation, and reviewed and approved the final version prior to publication).

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