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Personalized treatment and prophylactic strategies in pediatric patients from the Ukrainian familial hypercholesterolemia registry: a comprehensive study

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Familial hypercholesterolemia (FH) is a genetic disorder characterized by elevated low-density lipoprotein (LDL) levels, increasing the risk of premature cardiovascular disease. Personalized treatment strategies tailored to pediatric FH patients offer promising solutions for effective management.

This study **aimed** to develop and evaluate a personalized treatment and prophylactic program focused on managing lipid levels and reducing cardiovascular risks in children with FH.

Materials and methods. The study included 15 children aged 5–18 years diagnosed with FH. A comprehensive evaluation was conducted, assessing anthropometric data, dietary profiles, and compliance, quality of life, and physical activity energy expenditure (PAEE). An extended lipid profile analysis included ApoA1, ApoB, lipoprotein(a), and dp-ucMGP levels. Cardiovascular risks were evaluated using instrumental assessments. Patients were divided into age groups, and personalized interventions were implemented – medical nutrition therapy, pharmacotherapy (statins, Omega-3 fatty acids, ezetimibe), and lifestyle modifications. Statistical analysis was performed using SAS® OnDemand for Academics.

Results. A stepwise diagnostic and therapeutic algorithm for managing children with pediatric dyslipidemia was developed. Logistic regression analysis revealed statistical significance in personalized interventions, with a positive β coefficient of 1.34. The odds ratio for statins was 3.82, indicating that their inclusion increased the likelihood of achieving target LDL-C levels by nearly fourfold. PAEE showed a trend toward influencing LDL-C achievement.

Conclusions. Personalized treatment strategies, combining dietary correction and targeted pharmacotherapy, effectively improved lipid profiles and reduced cardiovascular risks in children with FH. Significant external factors impacting LDL-C targets were identified. This study highlights the importance of individualized approaches in pediatric FH care and underscores the need for further research.

This research was carried out in accordance with the principles of the Declaration of Helsinki. The study protocol was approved by the Local Ethical Committee. The informed consent was obtained from all participants.

No conflict of interest was declared by the authors.

Keywords: children, familial hypercholesterolemia, personalized treatment, lipid profile, cardiovascular risk, statins, dietary intervention, pediatric dyslipidemia.

Персоналізовані лікувально-профілактичні стратегії у пацієнтів дитячого віку з Українського реєстру сімейних гіперхолестеринемій: комплексне дослідження

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Сімейна гіперхолестеринемія (СГ) – це генетичне захворювання, що характеризується підвищеним рівнем ліпопротеїнів низької щільності (ЛПНЩ) та супроводжується підвищеним ризиком передчасних серцево-судинних захворювань. Персоналізовані стратегії лікування, адаптовані для дітей із СГ, відкривають перспективні можливості для ефективного контролю захворювання.

Мета дослідження – розробка та оцінка персоналізованої лікувально-профілактичної програми, спрямованої на корекцію ліпідного профілю та зниження серцево-судинних ризиків у дітей із СГ.

Матеріали та методи. У дослідженні взяло участь 15 дітей віком 5–18 років із встановленим діагнозом СГ. Проведено комплексну оцінку, яка охопила антропометричні вимірювання, аналіз харчового раціону та дієтичного комплаєнсу, оцінку якості життя та визначення енергетичних витрат на фізичну активність (PAEE). Розширений аналіз ліпідного профілю містив визначення рівнів ApoA1, ApoB, ліпопротеїну(а) та dp-ucMGP. Оцінку серцево-судинних ризиків проводили за допомогою інструментальних методів. Пацієнтів розподілили за віковими групами, після чого було впроваджено персоналізовані втручання – медичну дієтичну терапію, фармакотерапію (статини, омега-3 жирні кислоти, езетиміб) та модифікацію способу життя. Статистичний аналіз виконано за допомогою SAS® OnDemand for Academics.

Результати. Розроблено покроковий діагностично-лікувальний алгоритм ведення дітей із дисліпідемією. Логістичний регресійний аналіз виявив статистично значущий вплив персоналізованих втручань, водночас позитивний β-коефіцієнт становив 1,34. Відношення шансів для статинів було 3,82, що свідчить про майже чотириразове підвищення ймовірності досягнення цільових рівнів ЛПНЩ. PAEE демонстрував тенденцію до впливу на досягнення цільового рівня ЛПНЩ.

Висновки. Персоналізовані стратегії лікування, що поєднують корекцію харчування та цільову фармакотерапію, сприяли покращенню ліпідного профілю та зниженню серцево-судинних ризиків у дітей із СГ. Виявлено значущі зовнішні фактори, що впливали на досягнення цільових рівнів ЛПНЩ. Це підкреслює важливість індивідуального підходу до ведення дітей із СГ та необхідність подальших досліджень.

Дослідження виконано відповідно до принципів Гельсінської декларації. Протокол дослідження ухвалено Локальним етичним комітетом зазначеної в роботі установи. На проведення досліджень отримано інформовану згоду пацієнтів.

Автори заявляють про відсутність конфлікту інтересів.

Ключові слова: діти, сімейна гіперхолестеринемія, персоналізоване лікування, ліпідний профіль, серцево-судинний ризик, статини, харчова корекція, дитяча дисліпідемія.

Introduction

Preventing and managing atherogenic risk factors during childhood can significantly reduce the incidence of cardiovascular disease in adulthood [15].

A comprehensive review of international studies on the early detection and prevention of cardiovascular diseases highlights several screening algorithms for identifying children with atherogenic risk factors, particularly dyslipidemia [2,4,6,18].

Based on these insights, we developed a tailored, stepwise approach for managing Ukrainian pediatric patients with the goal of identifying children with atherogenic risk factors, including familial hypercholesterolemia (FH), and implementing timely treatment and preventive measures.

The aim of this study is to develop and evaluate a personalized treatment and prophylactic program focused on managing lipid levels and reducing cardiovascular risks in pediatric patients diagnosed with FH.

To achieve the outlined **objectives**, several key tasks were undertaken: auxological assessment of children with FH, analysis of their nutritional profiles and dietary compliance, evaluation of health-related quality of life (HRQoL), assessment of physical activity energy expenditure (PAEE), and analysis of their extended lipid profiles. Instrumental cardiovascular studies, including ECG, echocardiography, and triplex scanning of the common carotid artery to measure intima-media thickness and ankle-brachial index were also performed. Additionally, circulating levels of dephosphorylated-uncarboxylated matrix Gla-protein (dp-uc-MGP), a marker of vascular wall microcalcification, were determined.

The developed approach involves sequential steps that comprehensively integrate clinical, laboratory, and instrumental data to establish diagnosis and provide personalized recommendations tailored to each patient.

Materials and methods of the study

A retrospective study was conducted on pediatric patients from various regions of Ukraine who were treated at the Department of Cardiology of the Kyiv City Children's Clinical Hospital №1.

Inclusion criteria for the study were: a confirmed diagnosis of familial hypercholesterolemia for at least 6 months, age between 5 and 18 years, adherence to prescribed lipid-lowering therapy and an appropriate diet (CHILD-1) [4], signed informed consent of the child and parent(s) (or legal guardian(s)).

Exclusion criteria were withdrawal of informed consent, age less than 5 years, interruption of lipid-lowering therapy >1 month, presence of a condition other than FH causing lipid metabolism disorders (diabetes mellitus, hypothyroidism, nephrotic syndrome, chronic kidney disease, primary cholangitis, obstructive jaundice, obesity, Cushing's syndrome, pheochromocytoma, etc.); or intake of medications known to affect lipid metabolism (amiodarone, thiazide diuretics, beta-blockers, glucocorticoids, estrogens, androgens, immunosuppressants, anticancer agents, antipsychotics, HIV-1 protease inhibitors, anticonvulsants, retinoids, growth hormones and others).

A total of 118 children were assessed between January and December 2021, of whom 15 met the inclusion criteria and agreed to participate in the study. The informed consent was obtained from both the children and their parent(s) or legal guardian(s).

Children diagnosed with FH were included in the study group (hereinafter referred to as «FH patients» or «FH group») (n=15), with diagnoses established using the Dutch Lipid Clinic Network criteria [3]. The children's ages ranged from 5 to 17 years, with a gender distribution of 55% boys and 45% girls. The control group consisted of healthy peers (n=21). The children were stratified by age and sex, with age groups defined according to WHO guidelines: 5–9 years, 10–14 years, and 15–18 years. The groups were representative in terms of age and sex.

Blood samples were collected after an overnight fast (⩾8 hours) to measure total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C, calculated using Friedewald's formula) [13], high-density lipoprotein cholesterol (HDL-C), triglycerides (TG), apolipoprotein A1 (ApoA1), apolipoprotein B (ApoB), and lipoprotein (a). Non-HDL cholesterol was calculated as TC minus HDL-C. Remnant cholesterol (rC) was calculated as TC minus LDL-C minus HDL-C. Subjects' blood plasma was also used to quantify the inactive dephosphorylated-uncarboxylated (dp-uc) isoform of matrix Gla protein (IDS-iSYS InaKtif MGP® UK) on the IDS-iSYS Multi-Discipline Automated System.

The study was conducted in accordance with the Declaration of Helsinki and Convention on Human

Rights and Biomedicine, the Council of Europe, and Ukrainian laws governing research on human subjects.

Statistical analysis. Auxological parameters, including body weight, height, and body mass index (BMI), were measured in surveyed children using routine anthropometric methods. Additionally, carotid intima-media thickness (cIMT) and the ankle-brachial index (ABI) were assessed to evaluate vascular health. Electrocardiography (ECG) and echocardiography were also conducted on all subjects following standard protocols to assess cardiac function and structure.

The KINDL® questionnaire [16] and the Child/Youth Physical Activity Questionnaire (C(Y)PAQ) [1] were used to establish the quality of life and physical activity levels, respectively.

The KINDL® is a comprehensive tool for assessing HRQoL in children and young people aged 3 years and over. The KINDL® consists of 24 Likert scale items related to six modules: physical well-being, emotional well-being, self-esteem, family, friends, and daily activities (school or kindergarten). The subscales of these six modules were combined to produce an overall score. Participants answered questions on a 5-point Likert scale (0 = never, 1 = rarely, 2 = sometimes, 3 = often and 4 = always). All subscales were then converted into scores 0 to 100, where higher scores corresponded to a better quality of life index. Age-specific versions consider the changes in the quality of life dimensions in the course of child development.

The Children's Physical Activity Questionnaire (CPAQ) was administered to the youngest group (ages 5–9) and completed with partial parental help. The CPAQ questionnaire assesses the type, frequency, and duration of physical activity and sedentary behavior over the past 7 days. The Youth Physical Activity Questionnaire (YPAQ) was used among older children (10–14 years and 15–18 years). This tool allows us to determine the frequency and duration of 47 different activities on both weekdays and weekends during the past week. As such, the YPAQ assesses the mode, frequency, and duration of physical activity and sedentary behavior across all parameters, including school hours and free time over the past 7 days. Estimates of PAEE were derived from the CPAQ and YPAQ questionnaires. The calculation was based on the formula [1] used to estimate daily PAEE, according to accepted metabolic equivalent of task (MET) values [5]. PAEE levels were assessed according to the Sesso classification [17] as follows:

- low: <2,100 kilojoules per week (kJ/wk);
- low intermediate: 2,100–4,199 kJ/wk;
- intermediate: 4,200–8,399 kJ/wk;
- upper intermediate: 8,400–12,599 kJ/wk;
- high: ⩾12,600 kJ/wk.

Children with FH included in the study were interviewed using an adapted Food Frequency Questionnaire (FETA, FFQ EPIC Tool for Analysis® University of Cambridge) [14]. The interview was conducted with parents present as it was requested by all patients.

The FFQ EPIC Tool for Analysis® University of Cambridge Food Frequency Questionnaire is designed to measure the participant's usual food intake during the previous year. The main part of the questionnaire contains a list of the 130 most frequently and infrequently consumed food items. For each item on the list, participants are asked to indicate their usual frequency of consumption by selecting 1 of 9 frequency categories. Categories range from «never» or «less than once a month» to «6+ times a day». Portions are reported in units or usual portions (e.g., one apple, one slice of bread) or in household measures (e.g., glass, cup, spoon). Each item in the questionnaire was assigned an average portion size (this portion size is the same for all participants, regardless of their gender or age). The input data were processed in FETA® University of Cambridge [14].

Extended lipid profile data (TC, LDL-C, HDL-C, VLDL-C, TG, rC, non-LDL-C, apoA1, apoB, lipoprotein (a)) and dp-ucMGP level were analyzed with SAS® OnDemand for Academics (SAS Institute Inc, North Carolina, USA). Data were assumed to be normally distributed (verified analytically by Shapiro-Wilk, Kolmogorov-Smirnov, and graphically by Q-Q plot). Statistical significance was set at $p \leqslant 0.05$.

The interpretation of the results was based on the strength of the association, derived from the obtained Pearson correlation coefficient [9]. After analyzing the correlation matrix, all possible combinations of variables were considered to identify potential patterns and interactions. Based on the correlation matrix and the analysis of all variable combinations, a thorough selection of variables for further analysis was conducted. The variables were chosen based on their correlation strength, statistical significance, and relevance to the study's objec-

tives. Using logistic regression analysis, the relationship between mGla protein levels and the presence of a familial hypercholesterolemia diagnosis was investigated. The model's effectiveness was evaluated using the receiver operating characteristic (ROC) curve.

A stepwise multiple linear regression analysis was conducted to determine which variables significantly predict the mGla protein variable in both the FH and control groups, followed by an evaluation of the model's effectiveness. The overall significance of the logistic regression model was assessed using the Chi-square test (χ^2). Additionally, the β coefficient for statin therapy was examined to determine its direction and significance, with a particular focus on whether it demonstrated a positive association with achieving target LDL-C levels. The odds ratio for the statin variable was also calculated to quantify the magnitude of its effect.

A stepwise logistic regression analysis with inclusion was performed to examine the influence of variables on the target LDL-C level to predict the value of achieving the target LDL-C level in the FH group, assessing whether it showed a meaningful association.

Results of the study

Analysis of medical and family history

During the study, the medical and family history of each patient was thoroughly analyzed. This included identifying any family history of heart attack, treated angina, or interventions for ischemic heart disease (such as coronary artery bypass grafting, stenting, or angioplasty), as well as cases of sudden cardiac death or ischemic stroke before the age of 55 in male relatives (grandfather, father, uncle, brother) or before the age of 65 in female relatives (grandmother, mother, aunt, sister).

The diseases identified in the children of the main group provide a background for the development of secondary dyslipidemia, underscoring the need for more thorough examinations of patients with these conditions.

In all children with FH (n=15), a significant family history of the disease was identified, potentially increasing the risk of atherosclerosis development. The diagnosis of FH in the examined patients was validated using the Dutch Lipid Clinic Network criteria [3].

The significant findings in family history and medical history were incorporated into the developed management program for patients with dyslipidemia. This aimed to enhance differential diagnosis and create an individualized approach to pharmacological correction.

Auxological assessment of patients with dyslipidemia

Anthropometric data collected from children in the primary group at the time of diagnosis of dyslipidemia indicated that more than half of the children demonstrated harmonious growth. However, it is important to note that 35.59% of children were overweight, and 2.54% were obese, underscoring the necessity of including continuous auxological assessments for patients with dyslipidemia [11].

An evaluation of anthropometric measurements across different age groups in children with FH revealed that nearly 70% of children had harmonious physical development. Obesity was observed in every 5th child within the 5–9 and 15–18 age groups, while every 5th child in the 10–14 age group was underweight.

Assessment of dietary profile and dietary compliance

Based on the results of our study using the FFQ® questionnaire [11], the dietary profiles of patients with FH across all age groups were characterized by a high intake of energy-dense foods that were poor in essential nutrients, which are not recommended for this patient population.

A retrospective analysis of anthropometric data of FH patients at the time of establishing diagnosis revealed that 6.6% of the children were underweight (<-1z), 13.4% were overweight (>+1z), and 13.4% were obese (>+2z). After implementing the CHILD-1 diet for 6 months, 6.7% of the children were classified as severely underweight (<-2z), 20% as underweight (<-1z), 6.6% as overweight (>+1z), and 6.7% as obese (>+2z) (Figure 1).

The suboptimal physical development measures and changes in laboratory values prompted the initiation of medical nutrition therapy. Dynamic monitoring of the children with FH in the study showed improvements in physical development, with only about 13% remaining overweight or obese.

The study results indicate that children with FH across all age groups, both before and after starting the CHILD-1 diet, did not sufficiently meet their daily energy needs, with a deficit reaching 41.45%. This suggests that patients in all age groups struggle to maintain a balanced diet independently, resulting in disharmonious body mass. Consequently, they

require more meticulous medical supervision and regular monitoring by healthcare providers.

Despite the implementation of the CHILD-1 diet, it was not possible to achieve a complete balance of macronutrients, micronutrients, and vitamins across all age groups. The average daily intake of calories, proteins, fats, and carbohydrates did not meet age-specific requirements, nor did the intake of essential nutrients such as calcium, iodine, zinc, and vitamin D. The nature of these deficiencies varied across different age groups, indicating the need for a more individualized dietary approach to address the specific nutritional needs of children with FH. Assessment of adherence to dietary treatment revealed the most positive results in the 5–9 age group, which may be explained by the active involvement of parents in ensuring proper nutrition. The most imbalanced results were observed in the 10–14 age group, where the average daily intake of energy in kcal, proteins, fats, and carbohydrates did not meet age-specific needs and was characterized as insufficient. The 15–18 age group demonstrated a more conscious approach to diet adherence, yet their cholesterol intake still exceeded recommended levels.

Thus, patients with FH across all age groups require a personalized multidisciplinary approach to diet composition and nutritional support to achieve dietary compliance.

HRQoL and PAEE

Analysis of the KINDL® questionnaire data [8] indicated that the total quality of life score for patients with FH and their healthy peers did not differ statistically. In other words, the FH patients and the control group were equally satisfied with their quality of life. This suggests that children with FH perceived themselves as healthy or nearly healthy, and this underestimation of their condition may lead to lower compliance with recommended preventive and therapeutic measures. Consequently, children with FH may face significant health issues in the future, making the development of healthy behavior, education, and awareness crucial components of managing such patients.

It is important to highlight the strong negative correlation between the 'Self-Assessment' module and cholesterol intake as measured by the FFQ® (r=-0.89; p=0.01), suggesting an inverse relationship between cholesterol intake and the child's subjective self-assessment. Additionally, a strong positive correlation was observed between the 'Physical Well–Being' module and average daily energy intake (kcal) (r=0.73; p=0.03), indicating a potential direct link between caloric intake and the child's perception of their physical health. These findings could suggest that the child's view of their life is significantly influenced by their illness.

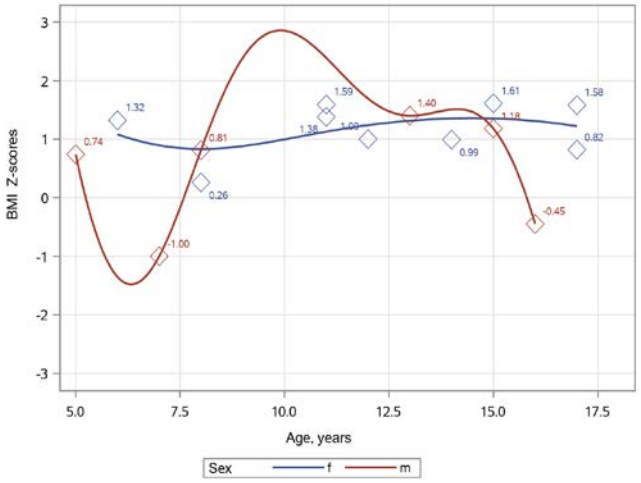

Fig. 1. Distribution of BMI z-scores (with regularized B-splines) of FH group by age and sex

Analysis of data from the C(Y)PAQ physical activity questionnaire data [8] showed that the 5–9 age group, with average energy expenditure, was the most physically active among all the children studied. In contrast, all other age groups exhibited average to low energy expenditure on physical activity, with a tendency towards lower levels. Among children with FH, partial Pearson correlation, controlling for body mass, revealed a strong negative correlation between age and PAEE (r=-0.73; p=0.02), indicating a trend towards decreased energy expenditure on physical activity with increasing age, regardless of body mass. Additionally, strong positive correlations were observed between PAEE and the 'Friends' module (r=0.76; p=0.02), as well as between PAEE and the total quality of life score (r=0.71; p=0.04). These findings suggest that external factors, such as peer interactions and perceived health status, may significantly influence the level of energy expenditure on physical activity.

The C(Y)PAQ physical activity questionnaire data indicate that all patients exhibit relatively low levels of energy expenditure on physical activity, which could negatively impact their physical and mental well-being, both now and in the future. This may reflect a broader lack of motivation among children in contemporary society to maintain an active

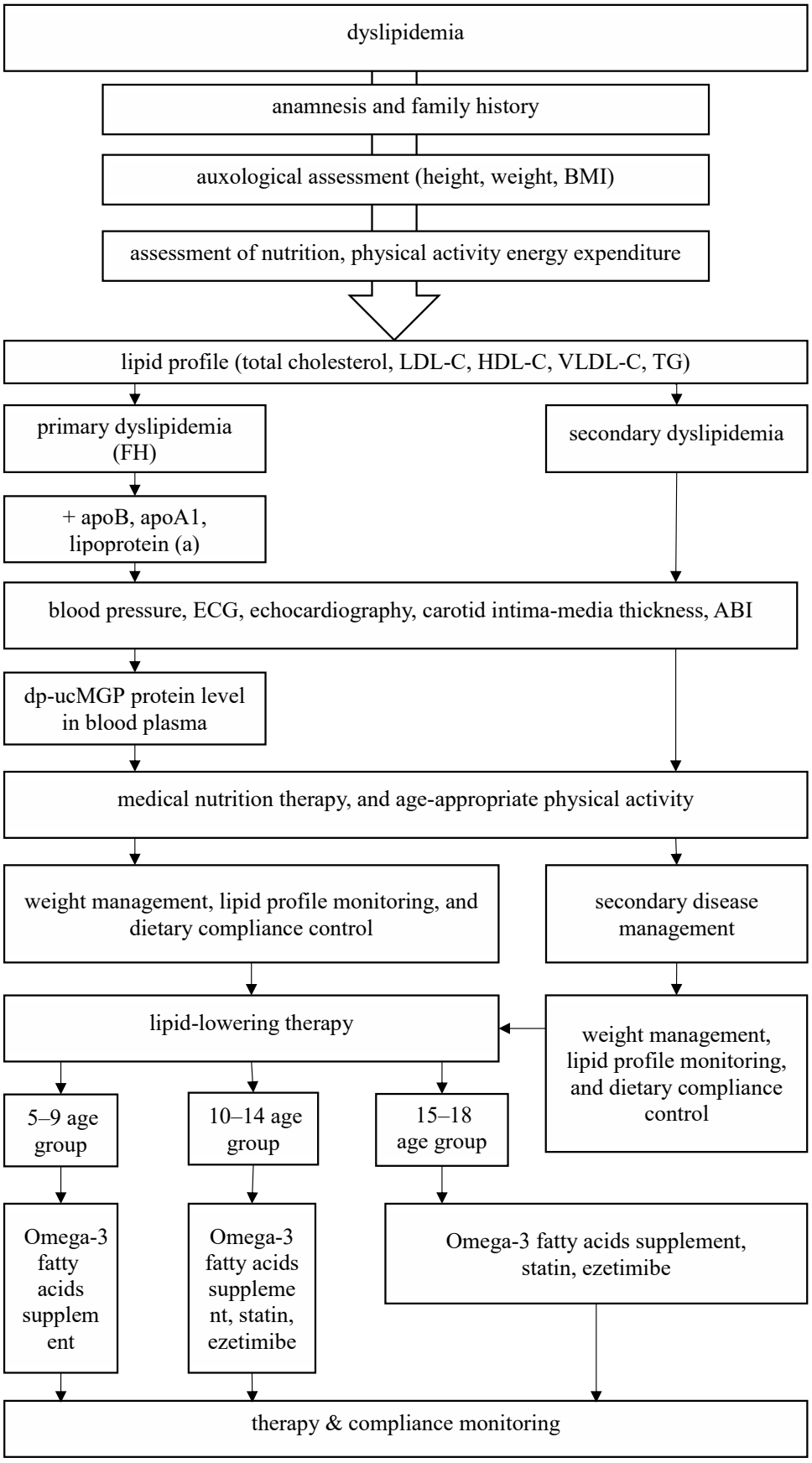

Fig. 2. Proposed stepwise algorithm for the diagnosis and management of dyslipidemia in children. ABI – ankle-brachial index

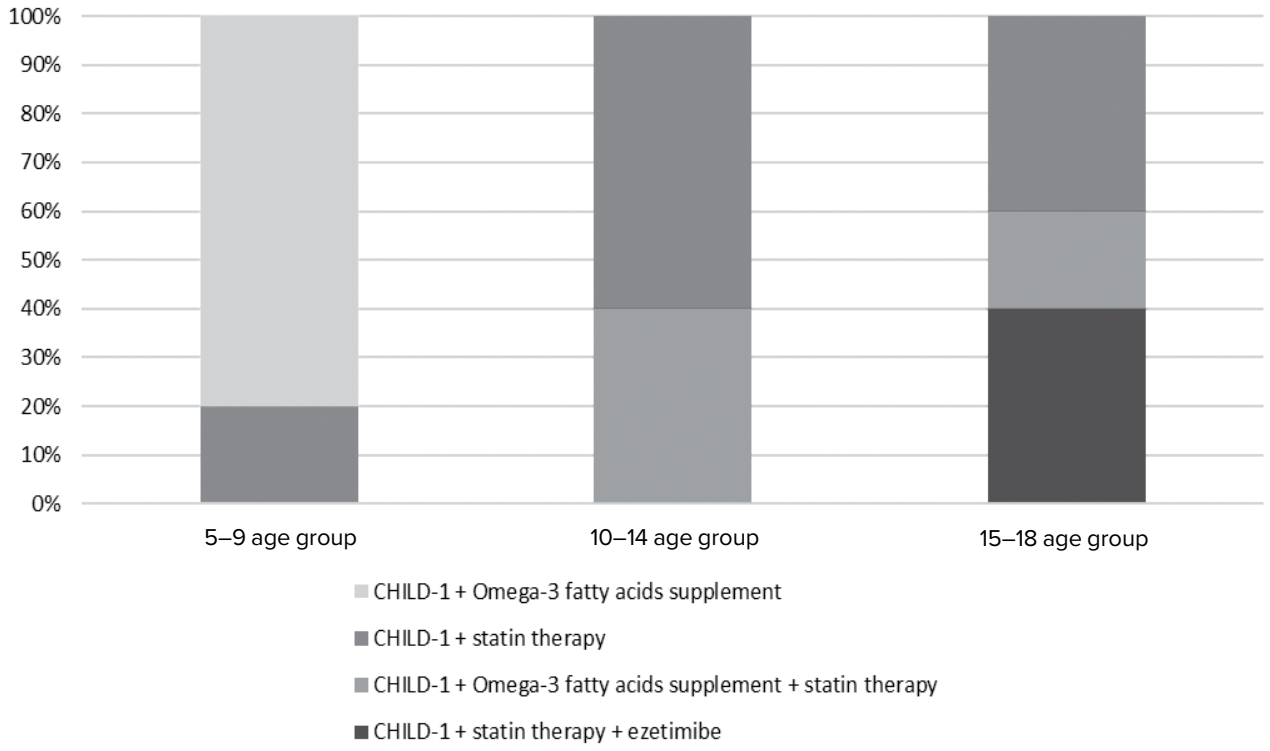

Fig. 3. Distribution of prescribed treatments by age group in children with FH, %

lifestyle. Given their increased cardiovascular risk, patients with FH are particularly vulnerable and require encouragement and support to meet the minimum necessary levels of physical activity.

Extended lipid profile, level of dp-ucMGP, and instrumental studies

Lipid profile changes in pediatric patients with FH were characterized as follows: in the 5–9 age group, elevated levels of LDL-C, non-HDL-C, and lipoprotein(a); in the 10–14 age group, elevated levels of LDL-C, TG, rC, non-HDL-C, and lipoprotein(a); and in the 15–18 age group, elevated levels of LDL-C, TG, non-HDL-C, and lipoprotein(a). The 10–14 age group showed the most pronounced dyslipidemic changes. All FH patients had significantly reduced apoA1 protein levels. Additionally, elevated lipoprotein(a) levels were observed across all age groups, highlighting its value as a marker for cardiovascular risk stratification in these patients. Therefore, assessing the extended lipid profile, including apoA1, apoB, and lipoprotein(a), in a single measurement is essential for managing children with FH [10].

In all age groups of children with FH, mGla protein levels were significantly elevated compared to the control group [10]. Measuring circulating mGla protein in pediatric FH patients can serve as a marker for vascular wall calcification. A threshold level of 751.49 pmol/L, with a sensitivity of 82.17% and specificity of 85.87%, effectively distinguishes FH patients from healthy peers [7], enabling the development of preventive strategies to mitigate vascular microcalcification. Additionally, assessing dp-ucMGP levels in FH patients as a predictor of vascular calcification may be a valuable supplementary method for reducing cardiovascular morbidity and mortality.

A multiple linear regression analysis was conducted to determine whether age and cholesterol intake according to FFQ® data significantly predict the mGla protein variable in children with FH.

The fitted regression model was as follows:

mGla protein level = 593.65 + 19.16 × (age) + + 0.70 × (cholesterol intake).

The regression model indicated that the predictors explained 91.01% of the variance, and a significant collective effect was found, $F=46.56$, $p<0.0001$, $R^2=0.91$. The individual predictors resulted in age ($\beta=19.16$, $t=4.23$, $p=0.0039$) and cholesterol intake ($\beta=0.70$, $t=5.13$, $p=0.0013$). No similar dependency was observed in the control group. It can be asserted that in our sample of children with FH, exposure to elevated cholesterol levels over a longer period is significantly associated

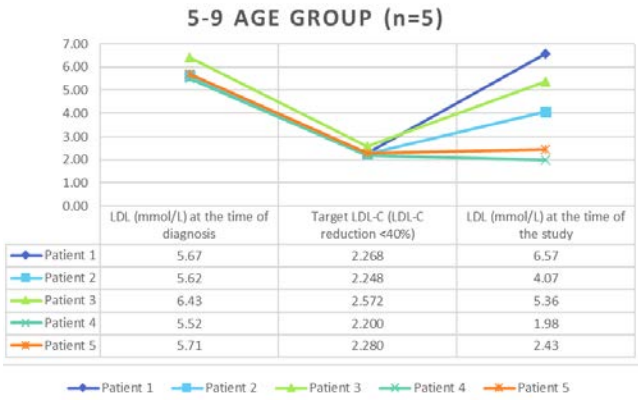

Fig. 4. Individual compliance of patients in the 5–9 age group with the target LDL cholesterol level

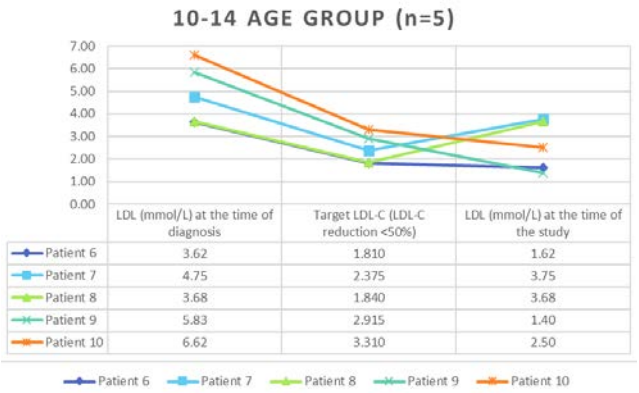

Fig. 5. Individual compliance of patients in the 10–14 age group with the target LDL cholesterol level

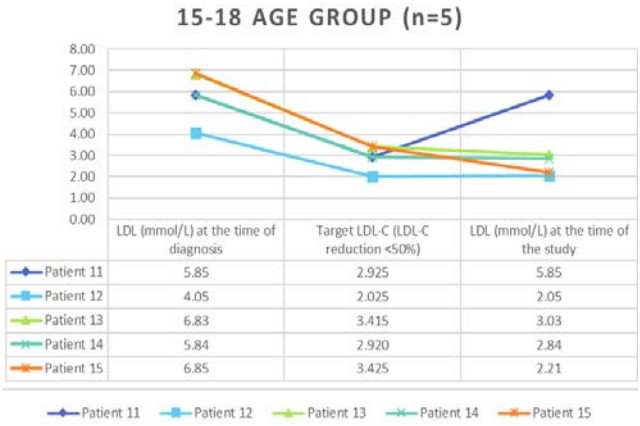

Fig. 6. Individual compliance of patients in the age group 15-18 years with the target LDL-C level

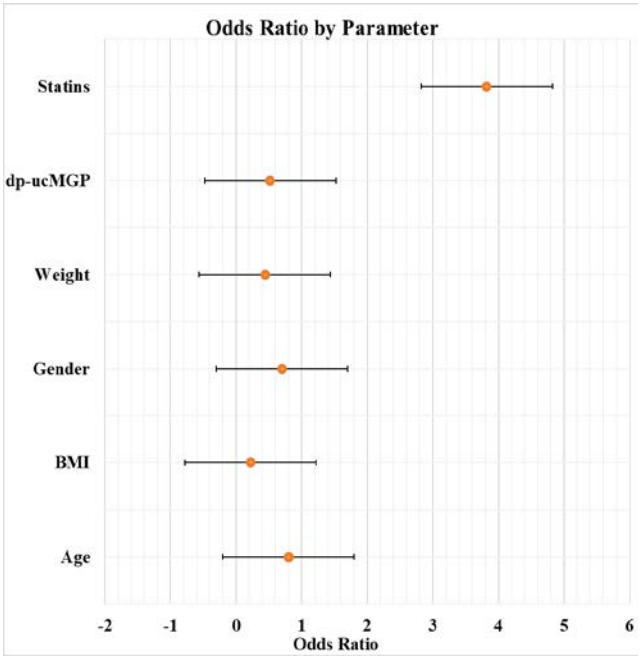

Fig. 7. Distribution of odds ratios in the model for predicting the achievement of the target LDL-C level variable

with higher levels of the vascular calcification marker, mGla protein [7,12].

In all age groups of children with FH and the control group, carotid artery intima-media thickness on both sides did not exceed the threshold level of 0.9 mm. However, a statistically significant difference in intima-media thickness on the left side was observed in FH children aged 15–18 (t=-3.08; p=0.001; 95% CI (-6.44; -0.84)) [10].

During the examination, no deviations from age-appropriate reference ranges were observed in any age group of children with FH regarding blood pressure, ECG, echocardiographic parameters, or the ankle-brachial index. This suggests the absence of macrovascular involvement or cardiac remodeling in our sample of FH patients.

Therefore, in diagnosing FH in children, lipid profile testing is essential, alongside medical history and cascade screening, as changes between ages 5 and 18 often remain subclinical and may not be detected through routine instrumental investigations, delaying preventive or therapeutic measures.

Treatment Protocol

Figure 2 provides a detailed illustration of the therapeutic and diagnostic interventions performed in this study [7].

All children with FH were prescribed the CHILD-1 diet as part of their therapeutic intervention [7]. According to AHA guidelines [6], HMG-CoA reductase inhibitors (statin) were introduced starting at age 8. Combination therapy with «statin + ezetimibe», which is FDA-approved [19] for children aged 10 and older and for girls who have reached menarche, was considered on a case-by-case basis. Figure 3 illustrates the distribution of prescribed treatments by age group for children with FH.

In the age group distribution, all children aged 5–9 were prescribed the CHILD-1 diet as part of their treatment. Additionally, 80% of patients in this age group followed the diet in combination with an Omega-3 fatty acid supplement, while 20% were treated with the diet alongside statin therapy.

All children in the 10–14 age group adhered to the dietary recommendations. 60% of these patients followed the diet alongside an HMG-CoA reductase inhibitor, while 40% were treated with the diet in combination with both an Omega-3 fatty acid supplement and statin.

All children in the 15–18 age group were prescribed the CHILD-1 diet. 40% of patients followed the diet alongside a statin. 20% adhered to the diet in combination with an Omega-3 fatty acid supplement and a statin, while 40% were treated with the diet, a statin, and a selective cholesterol absorption inhibitor (ezetimibe).

Target LDL-C levels for checking compliance were determined in relation to the child's age [4,6]. Figure 4 demonstrates individual compliance with LDL-C target levels after the introduction of dietary changes and treatment in the 5–9 age group.

In the 5–9 age group, only 20% of patients achieved the target LDL-C value. This outcome occurred despite meeting dietary compliance with a daily cholesterol intake of <300 mg/day, ensuring adequate protein intake, exceeding the recommended amounts of fats and carbohydrates as outlined by the CHILD-1 diet, and maintaining an intermediate level of PAEE.

In the 10–14 age group, 60% of patients with FH reached the target LDL-C value (Figure 5). In this age group, dietary compliance with a daily cholesterol intake of <300 mg/day was achieved. However, the diet provided insufficient proteins, fats, and carbohydrates compared to the CHILD-1 recommendations, and a low-intermediate level of PAEE was observed.

In the 15–18 age group, 60% of children with FH achieved the target LDL cholesterol values (Figure 6). However, in this age group, dietary compliance with a daily cholesterol intake of <300 mg/day was not met. The diet provided adequate levels of proteins, fats, and carbohydrates relative to the CHILD-1 recommendations, and a medium-low level of PAEE was observed.

A stepwise logistic regression analysis with inclusion was performed to examine the influence of the variable «statin therapy» in the treatment protocol on the variable «target LDL-C» to predict the value of «achieving the target LDL-C». The logistic regression analysis showed that the model as a whole was statistically significant ($\chi^2(3)=7.07$, $p<0.01$, $n=15$), with a positive β coefficient of 1.34 ($p=0.02$). The odds ratio for the statin variable was 3.82 (Figure 7).

Thus, it can be concluded that the presence of statins in the treatment protocol increased the probability that the dependent variable has the value «achievement of the target LDL-C level» by 3.82 times. The variable «PAEE» showed a tendency to influence the achievement of the target LDL-C level variable ($p=0.14$) [7].

Conclusion

The study developed a personalized treatment and prophylactic program aimed at managing lipid levels and reducing cardiovascular risks in pediatric patients with FH. The comprehensive approach, which included detailed assessments of dietary habits, physical activity, quality of life, and extended lipid profiles, allowed for the creation of a tailored diagnostic and therapeutic algorithm with consistent implementation of personalized interventions, combining medical nutrition therapy, pharmacotherapy, and lifestyle modifications.

The results demonstrated the statistical significance of personalized interventions, as evidenced by the logistic regression analysis. Notably, the inclusion of statins in the treatment protocol was associated with a 3.82-fold increase in the likelihood of achieving target LDL-C levels, highlighting their critical role in managing FH in children. While the physical activity energy expenditure variable did not reach statistical significance, it showed a trend toward influencing LDL-C management, suggesting that physical activity may still play an important supportive role in the overall treatment strategy.

The study underscores the importance of early diagnosis and personalized treatment strategies in pediatric FH management to prevent future cardiovascular complications and emphasizes the need for continued research to further refine these approaches. Ultimately, such efforts can contribute to improved long-term health outcomes for children with FH.

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