

Grażyna Odrowąż-Sypniewska¹, Magdalena Krintus¹, Joanna Siódmiak¹, Iwona Jaszowska², Radosława Staszak-Kowalska², Anna Zawadzka-Krajewska³, Szymon Kierat³, Urszula Demkow⁴

¹Department of Laboratory Medicine, Nicolaus Copernicus University Collegium Medicum, Bydgoszcz, Poland

²Department of Pediatrics, Pneumology and Allergology, Children's Hospital, Bydgoszcz, Poland

³Department of Pediatrics, Pneumology and Allergology Medical University of Warsaw, Poland

⁴Department of Laboratory Diagnostics and Clinical Immunology, Medical University, Warsaw, Poland

Serum 25(OH)D status and lipid profile in children with newly diagnosed asthma

ABSTRACT

Corresponding author:

Grażyna Odrowąż-Sypniewska, PhD, Prof.
Department of Laboratory Medicine,
Collegium Medicum, Nicolaus
Copernicus University
Sklodowskiej-Curie No. 9, 85–094 By-
dgoszcz, Poland
Phone + 48 52 585 40 46
Fax + 48 52 585 36 03
E-mail: odes@cm.umk.pl

Background. The problem of the influence of hyperlipidemia on asthma was addressed several years ago. Systematic review and meta-analysis performed in the pediatric population on the association between vitamin D status and lipid profile components revealed discordant results and indicated that higher serum 25(OH)D is related to a more favorable lipid profile.

Objective. We aimed to elucidate whether there was an association between vitamin D status and lipid profile components and apolipoprotein B in a sample of children with newly diagnosed atopic asthma.

Methods. The study included 150 children aged 2–12 years. Atopic asthma was diagnosed in 110 children; 40 children constituted a reference group. Fasting blood was collected to measure 25(OH)D total, lipid profile and apolipoprotein B concentrations.

Results. Children with asthma had significantly lower 25(OH)D ($p < 0.0001$) but similar lipid and apolipoprotein B concentrations. The proportions of hypercholesterolemia, hypertriglyceridemia and increased apoB concentrations were similar in both groups. HDL-C concentrations in asthmatic 25(OH)D-deficient children were higher compared with the children with sufficient levels ($p = 0.05$). ApoB concentration was lower in 25(OH)D-deficient compared with vitamin D sufficient asthmatics ($p = 0.0008$). Correlations between 25(OH)D concentration and lipids and apoB in asthmatics revealed gender differences. An inverse relationships between vitamin D and total cholesterol and HDL-C ($R = -0.39$, $p < 0.05$; $R = -0.475$, $p < 0.001$) were found in girls. In boys vitamin D correlated with LDL-C and apoB ($R = 0.376$, $R = 0.498$; $p < 0.001$).

Conclusion. In children with asthma lower 25(OH)D had more favorable gender-dependent effect on the lipid profile. The association of serum 25(OH)D and lipid levels in children with asthma remains for further studies.

Key words: 25-hydroxyvitamin D, asthma, lipids, apolipoproteins

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Introduction

A recent systematic review and meta-analysis performed in the pediatric population on the association between vitamin D status and lipid profile components have indicated that higher serum 25(OH)D is related to a more favorable lipid profile [1]. In a nationwide study in the Middle East and North Africa, performed in the pediatric population, a weak but significant inverse relationship of 25(OH)D with blood pressure, total cholesterol (TC), and LDL-cholesterol (LDL-C) was found. The association of vitamin D with HDL-cholesterol (HDL-C) was significantly positive [2]. Another earlier study reported that low serum 25(OH)D in children was

associated with high triglyceride (TG) levels [3]. Similar findings were reported in obese adults, showing 25(OH)D deficiency related to lower HDL-C and higher TG [4]. On the other hand, the associations in children were different. Delvin et al. reported no association in boys but the positive relationship between 25(OH)D and total cholesterol, triglycerides and apolipoproteins A1 and B in girls [4].

The problem of the influence of hyperlipidemia on asthma was addressed by Al-Shawwa et al. nearly 10 years ago [5]. In this study, the effect of serum cholesterol concentration on asthma frequency in children and adolescents was evaluated. It was found that hypercholesterolemia, independently of obesity,

increased the probability of asthma. A recent study in children with asthma has shown that higher LDL-cholesterol levels were associated with asthma occurrence and this association was amplified by overweight and obesity [6]. This finding is inconsistent with the earlier data indicating no association of apoB concentration with symptoms of asthma or allergy [7]. Having these controversies in mind, we aimed to elucidate whether there was an association between vitamin D status and lipid profile components and apolipoprotein B in a sample of children with newly diagnosed atopic asthma.

Methods

Study participants

The study included 110 children aged 2–12 years referring to the Department of Pediatric Pulmonology and Allergology at the Medical University (Warsaw, Poland) due to asthma-like symptoms. The subjects were recruited from October until April in the years 2012 and 2013. The written informed parental consent for each participant was obtained and the study protocol was approved by the Bioethics Committee at the Collegium Medicum of the Nicolaus Copernicus University. The diagnosis or exclusion of asthma were performed by an experienced pediatric pulmonologist as described previously [8]. All children included in the study did not receive any additional vitamin D supplementation beyond their regular dietary intake.

Atopic asthma was diagnosed in 110 children. The reference group included 40 children referring to the Outpatient Clinic for a routine check-up; in those children asthma and allergy were excluded by an experienced pediatrician on the basis of their medical history. Children who had any underlying liver, kidney, endocrine diseases or were on drugs/supplements that might affect vitamin D levels were excluded from the study. In all subjects body mass index (BMI) was calculated. Overweight or obesity were established on the basis of BMI-for-age percentiles for girls or boys [9]. Children with BMI between 85th–95th percentile were considered overweight, while those with BMI > 95th percentile were considered obese.

Sample collection and laboratory measurements

Fasting blood was collected in the early morning (7.00–9.00 a.m.). Serum was obtained within 1 h and stored deep-frozen (–80°C) until assayed. Serum total cholesterol (TC), low-density lipoprotein-cholesterol (LDL-C), high-density lipoprotein-cholesterol (HDL-C), triglycerides (TG), apolipoprotein B (PENTRA 400, Hori-ba ABX, Montpellier, France) and 25(OH)D total (EIA, IDS Ltd, Boldon, UK) were measured. 25-hydroxyvita-

min D EIA test kit, used in this study, is aligned with the ID-LC-/MS/MS Reference Measurement Procedure. The detection limit for 25(OH)D was 2.5 ng/mL.

We accepted the following cut-off values for normal lipids and apolipoprotein B: TC ≤ 170 mg/dL, HDL-C ≥ 45 mg/dL, LDL-C ≤ 110 mg/dL, TG ≤ 75 mg/dL up to 9 years of age, ≤ 90 mg/dL from 10 years of age, apoB < 0.75 g/L [4]. Serum 25(OH)D concentration ≥ 30 ng/mL was accepted as sufficient, 21–29 ng/mL as insufficient and ≤ 20 ng/mL as deficient, according to the recommendations for the Polish population [10].

Statistical analysis

We used descriptive statistics to obtain the characteristics of the study and reference groups. Continuous variables were expressed as mean ± standard deviation (Gaussian distribution) and median with 25th and 75th percentiles (non-Gaussian distribution). The data were compared using the Student's t-test for normally distributed variables and the Mann-Whitney U-test for non-normally distributed variables. The Spearman or ANOVA correlations were used to analyze the associations between variables. A p value < 0.05 was considered statistically significant. The statistical analysis was performed using Statistica 10.0 for Windows (StatSoft, Tulsa, OK, USA) and MedCalc 12.7.0 (MedCalc Software, Ostend, Belgium).

Results

Serum 25(OH)D was significantly lower in children with atopic asthma compared with the reference group, however, vitamin D deficiency was not a characteristic feature of asthmatics. The mean concentrations of lipids and apolipoprotein B concentrations were similar in both groups. The main features in children with asthma and the reference group were borderline (0.75– < 1.0 g/L) or unfavorable (≥ 1.0 g/L) apoB concentration (58% and 66%) and hypercholesterolemia (46.8% and 51%, respectively) (Tab. 1).

The comparison of median lipid and apoB values in relation to 25(OH)D concentration in asthmatic children is presented in Table 2. We found significantly higher HDL-C concentrations in 25(OH)D-deficient children compared with those with sufficient levels (p = 0.05). ApoB concentration was significantly lower in 25(OH)D-deficient compared with vitamin D sufficient children (p = 0.0008).

Bivariate correlation analysis between 25(OH)D concentration and lipids and apoB in asthmatics revealed gender differences. We found weak but significant inverse relationships between vitamin D and total cholesterol and HDL-C (R = –0.39, p < 0.05; R = –0.475,

Table 1. Biochemical and clinical characteristics of the study participants

Variable	Atopic asthma (n = 110)	Reference group (n = 40)	p value
Gender M/F (%)	53.4/46.6	57.1/42.9	0.600
Age (years)	5.0 (4.0–7.5)	4.5 (3.8–7.0)	0.13
25(OH)D [ng/mL]	27.7 ± 8.3	35.4 ± 13.04	< 0.0001
25(OH)D ≤ 20 ng/mL	18.2	10.0	0.127
Overweight/obesity (%)	10.0/11.2	2.1/2.0	0.04/0.04
Total cholesterol [mg/dL]	171 ± 33	175 ± 28	0.42
TC > 170 mg/dL (%)	46.1	51.0	0.836
LDL-C [mg/dL]	101 ± 28	108 ± 24	0.16
LDL-C > 110 mg/dL (%)	33.7	36.7	0.560
HDL-C [mg/dL]	54 ± 12	54 ± 0	0.73
HDL-C < 45 mg/dL (%)	21.3	18.4	0.326
TG [mg/dL]	71 ± 40	74 ± 31	0.73
Hypertriglyceridemia (%)	28.1	42.9	0.06
ApoB [g/L]	0.83 ± 0.17	0.85 ± 0.20	0.55
ApoB > 0.75 g/L (%)	58.0	66.0	0.56

BMI — body mass index; 25(OH)D — 25-hydroxyvitamin D; TC — total cholesterol; LDL-C — low-density lipoprotein cholesterol; HDL-C — high-density lipoprotein cholesterol; apoB — apolipoprotein B

Table 2. The comparison of selected biochemical and anthropometric indices in relation to 25(OH)D concentration in children with atopic asthma

Variable	25(OH)D deficiency (≤ 20 ng/mL) ^A	25(OH)D insufficiency 21–29 (ng/mL) ^B	25(OH)D sufficiency (≥ 30 ng/mL) ^C	p value	Post hoc
Age (years)	6.0 (5.0–8.5)	6.0 (4.0–7.0)	4.5 (4.0–7.0)	0.007	A v. C, p = 0.002
BMI [kg/m ²]	15.6 (14.6–16.0)	16.1 (15.2–17.4)	16.0 (15.0–17.0)	0.019	A v. C, p = 0.019
25(OH)D [ng/mL]	17.3 ± 2.4	24.2 ± 2.6	36.8 ± 5.4	< 0.0001	A v. B; A v. C; B v. C p < 0.0001
TC [mg/dL]	158 (147–164)	156 (134–174)	153 (137–170)	0.925	–
LDL-C [mg/dL]	86 (76–100)	93.5 (79–106)	100 (80–128)	0.137	–
HDL-C [mg/dL]	58 (56–66)	56 (52–66)	53 (48–62)	0.048	A v. C, p = 0.050
TG [mg/dL]	55 (45–68)	58 (47–70)	55 (45–68)	0.432	–
ApoB [g/L]	0.72 (0.68–0.76)	0.82 (0.71–0.93)	0.87 (0.75–1.03)	0.008	A v. C, p = 0.0008 A v. B, p = 0.09

A — children with 25(OH)D < 20 ng/mL; B — children with 25(OH)D 20 to ≤ 30.0 ng/mL; C — children with 25(OH)D > 30 ng/mL; 25(OH)D — 25-hydroxyvitamin D; ApoB — apolipoprotein B; BMI — body mass index; HDL-C — high-density lipoprotein cholesterol; LDL-C — low-density lipoprotein cholesterol; TC — total cholesterol; TG — triglycerides

p < 0.001) in girls. In boys vitamin D correlated with LDL-C and apoB and these relationships were positive (R = 0.376, R = 0.498; p < 0.001).

Discussion

Vitamin D status and its association with lipids in children has not been extensively studied yet and the findings

are controversial. Similarly, the associations of asthma with hyperlipidemia were not only diverse but also were affected by the presence of overweight and obesity. The underlying mechanisms still remain to be elucidated. We evaluated the association between vitamin D status and lipid profile components and apolipoprotein B in a sample of children with newly diagnosed atopic asthma.

Unexpectedly, we found that vitamin D-deficient asthmatic children had a more favorable lipid profile

(significantly higher HDL-cholesterol and lower apoB levels) than children with vitamin D sufficiency. Median value of LDL-cholesterol was also lower in 25(OH)D-deficient children but the difference did not reach statistical significance. These findings were supported by significant positive correlations of vitamin D with LDL-cholesterol and apoB concentrations observed in boys and a significant inverse relationship of vitamin D with HDL-cholesterol observed in girls.

Our findings are inconsistent with some recent data based on the systematic review and meta-analysis performed on the association of vitamin D with lipids in the pediatric population [1]. On the other hand, they are similar to the data reported earlier by Delvin et al. [4]. We have observed, however, the positive associations of vitamin D with lipids and apoB in boys, whereas they have found no associations in boys but only in girls [4]. They suggested that such gender differences in lipid metabolism may be due to the different effects of sex hormones [4, 11]. In fact, Delvin et al. included the French-Canadian children and adolescents in their study of whom more than 60% were over 13 years old, whereas in our study, the children were much younger and less than 20% were in the pubertal stage (girls 8–12 years, boys 10–12 years old).

In a recent study of Argentinean children, severe vitamin D deficiency was shown to be associated with an increased serum apoB concentration [12]. These findings do not match the results of this study, in which lower apoB was observed in 25(OH)D-deficient children. Notably, the children in our study showed only very low percentage presented with severe vitamin D deficiency < 15 ng/mL (6.4%), whereas in the Argentinian population severe vitamin D deficiency was found in almost 79% of cases. The results of our own study are consistent with those recently reported by Ashraf et al., which suggested a possible role of vitamin D on apolipoprotein synthesis [13], and with those published earlier by Teramoto et al. explaining the binding of vitamin D to LDL particles [14].

In children with asthma higher LDL-C levels were associated with the occurrence of asthma and this association was amplified by overweight and obesity [6]. Among children with asthma in our study the percentage of overweight and obesity was 21.2%, which could affect lipid metabolism only to a minor extent. It is known that the excess body fat leads to the increased storage of vitamin D in the adipose tissue and reduces its serum concentration and availability. However, it was shown that although serum 25(OH)D levels may be lower, the concentration of bioavailable one may not be low due to a lower concentration of vitamin D binding protein (VDBP) [15]. We did not measure the concentration of

VDBP and this, besides the limited number of participants, constitutes a limitation of our study.

Finally, we conclude that in children with newly diagnosed yet untreated atopic asthma lower 25(OH)D had more favorable effect on the lipid profile and this effect was gender-dependent. However, the association of serum 25(OH)D and lipid levels and the underlying mechanisms in children with asthma are not clear and remain for further studies.

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