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CLINICAL STUDY

# Ratio of lipid parameters to coenzyme $Q_{10}$ could be used as biomarker of the development of early complications of obesity in children

Gvozdjakova A[1], Kucharska J[1], Tkacov M[1], Singh RB[2], Hlavata A[3]

*Comenius University, Medical Faculty, Pharmacobiochemical Laboratory of Third Medical Department, Bratislava, Slovakia.* **anna.gvozdjakova@fmed.uniba.sk**

**Abstract:** *Background*: Chronic obesity is associated with reduced levels of antioxidants, increased free oxygen radicals, and oxidative stress. Child obesity may lead to the development of complications, such as changes in metabolism, metabolic syndrome, neurological, cardiological, respiratory, renal, gastrointestinal, endocrinological, and musculoskeletal conditions.
*The aim* of the present study is to establish whether there is a correlation between basal $CoQ_{10}$ plasma concentration and the ratio of lipid parameters to $CoQ_{10}$ in obese children.
*Methods*: The study included 101 obese children and 20 non-obese children, aged 10 – 18 years. Antioxidants – $CoQ_{10\text{-}OX}$, α-tocopherol, β-carotene – in plasma were measured by HPLC method with UV detector, and plasma malondialdehyde spectrophotometrically.
*Results:* High correlation was found between plasma concentration of $CoQ_{10}$ and the ratio of total Chol/$CoQ_{10\text{-}OX}$ as well as between $CoQ_{10\text{-}OX}$ and the ratio of HDL Chol/$CoQ_{10}$ in plasma of obese children. The lowest correlation was between plasma concentration of $CoQ_{10\text{-}OX}$ and the ratio of LDL Chol/$CoQ_{10}$ , as well as between $CoQ_{10\text{-}OX}$ and the ratio of TAG/$CoQ_{10}$ in obese children.
*Conclusion*: An increase of the ratios of lipid parameters to $CoQ_{10}$ is associated with child obesity and could be used as biomarkers of early complications in the development of obesity in children *(Tab. 3, Fig. 5, Ref. 22)*.
Full Text in free PDF *www.bmj.sk*.
Key words: child obesity, coenzyme $Q_{10}$, ratio of lipid fractions/coenzyme $Q_{10}$.

Obesity is characterized by excessive deposition of fat, with a surplus of adipose tissue in relation to other tissues of the organism. The prevalence and magnitude of childhood obesity are increasing dramatically. Due to complications, over one million obese people die each year in Europe (1). Several factors contribute to the development of obesity, as inactivity, high calorie diet, some drugs, age, stress, sleep deficit, and family history.

Chronic obesity may lead to complications, such as changes in metabolism, metabolic syndrome, neurological conditions (risk of stroke, depression, reduced quality of life), cardiological derangements (hypertension, left ventricular hypertrophy, risk of coronary disease, endothelial dysfunction), respiratory ailments (asthma), renal defects (proteinuria), gastrointestinal affections (liver fibrosis, liver steatosis), endocrinological disorders (diabetes, hypogonadism in boys, stress incontinence), and musculoskeletal pathology (fractures, risk of degenerative joint disease). Metabolic syndrome often occurs in obese children and adolescents and deteriorates with increasing obesity (2). Obesity associated with reduced levels of antioxidants may contribute to a deficient protection of low-density lipoproteins (LDL) (3). In obese children significantly higher total cholesterol and LDL-cholesterol were documented in comparison with non-obese children, although these parameters were on the highest reference levels (4). High fat deposition in the organism produces increased free oxygen radicals, oxidative stress (5, 6, 7), which is a key factor in the pathogenesis of metabolic syndrome and may contribute to insulin resistance (8).

Coenzyme $Q_{10}$ ($CoQ_{10}$) is known to be an effective inhibitor of oxidative damage to LDL. In some cases, complications of obesity may be associated with impaired energy production and with deficiency of coenzyme $Q_{10}$. Coenzyme Q, ubiquinone or vitamin Q, is a lipid-soluble compound existing in all cell membranes. Coenzyme Q has several metabolic functions. It is an essential cofactor for ATP production in the inner mitochondrial membrane, a carrier of electrons and protons in the respiratory chain coupled to ATP synthesis. $CoQ_{10}$ in reduced form (ubiquinol) acts as an antioxidant, inhibiting lipid peroxidation in biological membranes. As an antioxidant it may regenerate other antioxidants, change

[1]Comenius University, Medical Faculty, Pharmacobiochemical Laboratory of Third Medical Department, Bratislava, Slovakia, [2]Halberg Hospital and Research Institute, Moradabad, India, and [3]Comenius University in Bratislava, Medical Faculty, Second Children Hospital, Metabolic Department, Bratislava, Slovakia

**Address for correspondence:** A. Gvozdjakova, Comenius University in Bratislava, Medical Faculty, Pharmacobiochemical Laboratory of Third Medical Department, Sasinkova 4, SK-811 05 Bratislava, Slovakia.
Phone/Fax: +421.2.59357242

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**Tab. 1. Body weight in non-obese and obese children.**

| Boys | | | Girls | | |
|---|---|---|---|---|---|
| Age [years] | Non-obese [kg/bw] | Obese [kg/bw] (%) | Age [years] | Non-obese [kg/bw] | Obese [kg/bw] (%) |
| 10 | 35.81 | 62.20 (+73.7) | 10 | 35.66 | 67.30 (+88.7) |
| 11 | 39.43 | 68.46 (+73.6) | 11 | 41.32 | 73.58 (+78.1) |
| 12 | 44.30 | 86.50 (+95.3) | 12 | 45.54 | 79.00 (+73.5) |
| 13 | 50.52 | 87.83 (+73.8) | 13 | 50.54 | 77.30 (+52.9) |
| 14 | 56.15 | 82.40 (+46.7) | 14 | 52.28 | 95.70 (+83.0) |
| 15 | | | 15 | 55.74 | 85.90 (+54.1) |
| 16 | 66.14 | 129.70 (+96.6) | 16 | 57.31 | 95.13 (+66.0) |
| 17 | 69.16 | 119.63 (+73.0) | 17 | 53.58 | 98.70 (+84.2) |

tocopheryl radical to tocopherol, protect mitochondrial proteins of the inner membrane and DNA against oxidative damage, and can stimulate cell growth and inhibit cell death. Decreased biosynthesis or increased degradation of $CoQ_{10}$ may cause several deficiencies in the organism. In healthy individuals, $CoQ_{10}$, is synthetized in physiological concentrations in cells, however in diseases or in ageing low levels of $CoQ_{10}$ were found (9, 10). CoQ synthesis has a key function in adipose tissue differentiation, as a new regulator of adipose biology (11). The importance of $CoQ_{10}$ plasma and tissue levels in obesity and in obesity complications has not yet been completely elucidated.

*The aim* of the present study is to estimate basal values of plasma antioxidants, lipid peroxidation and lipid parameters of non-obese and obese children and to establish whether there is a correlation between basal $CoQ_{10}$ plasma concentration and the ratio of lipid parameters to $CoQ_{10}$ concentration in obese children.

## Subjects and methods

The study included 101 obese children from various regions of Slovakia, aged 10–18 years (mean age: 12.58±2.26 years). The number of boys was 52 and of girls 49. *Body mass index* (BMI) was measured in all children. BMI in control children is between 25 and 85 percentil, in overweight children BMI is 90 percentil, and in obese children BMI is over 97 percentil.

This study includes only obese children, divided into three groups by using standard deviation (SD): moderate obesity by BMI from +2 to +4 SD, medium obesity by BMI from 4+ to 6+ SD, heavy obesity by BMI over +6 SD. *Antropometric characteristic* of 101 obese children: Children were divided by age into two groups: a) 10–13.99 years, BMI=30.01±3.9, b) 14–18 years, BMI=34.00±4.46.

In all children antropometric parameters, as body weight, height of body, circle of head, waist circumference, hips, midle circle of arm, thickness of cutaneous skinfolds were measured (12). The included criteria for obesity in children were significant differences in antropometric parameters, increased body weight and fatty tissue in comparison with the control group (non-obese children). The number of non-obese children was 20, aged 10–18 years (mean age: 14.25±1.88 years, 11 boys and 9 girls). Antioxidants – $CoQ_{10\text{-}OX}$, α-tocopherol, β-carotene – in plasma were measured by HPLC method with UV detector at 275 nm, 295 nm and 450 nm (13, 14). Plasma lipid peroxidation (measured as malondialdehyde production) was determined by the reaction with thiobarbituric acid spectrophotometrically at 532 nm (15), total cholesterol, HDL-cholesterol and triacylglycerols were assessed by a colorimetric method. For statistical evaluation unpaired Student´s t-test was used. Values $p<0.05$ were considered statistically significant.

**Tab. 2. Antioxidants and peroxidation of lipids in plasma of obese and non-obese children. Legends: $CoQ_{10}$ – coenzyme $Q_{10}$, MDA – malondialdehyde, P – statistical parameter.**

| **$CoQ_{10}$** [μmol/l] | Reference values | Non-obese children | Obese | |
|---|---|---|---|---|
| | | | Boys | Girls |
| mean | 0.40–1.00 | 0.77 | 0.37 | 0.31 |
| SD | | 0.12 | 0.03 | 0.02 |
| n | | 20 | 49 | 52 |
| P vs Non-obese | | | <0.0001 | |
| % vs Non-obese | | 100 | -52.21 | -59.74 |
| **α-tocopherol** [μmol/l] | | | **Children** | |
| mean | 15–40 | 19.15 | 20.95 | |
| SD | | 9.06 | 12.39 | |
| n | | 20 | 101 | |
| P vs Non-obese | | | NS | |
| % vs Non-obese | | 100 | +9.40 | |
| **β-carotene** [μmol/l] | | | **Children** | |
| mean | 0.3–3.0 | 1.99 | 2.40 | |
| SD | | 1.12 | 3.18 | |
| n | | 20 | 101 | |
| P vs Non-obese | | | NS | |
| % vs Non-obese | | 100 | +20.60 | |
| **MDA** [μmol/l] | | | **Children** | |
| mean | <4.5 | 4.52 | 6.53 | |
| SD | | 0.58 | 0.82 | |
| n | | 20 | 101 | |
| P vs Non-obese | | | <0.0001 | |
| % vs Non-obese | | 100 | + 44.47 | |

## Results

Table 1 shows obesity in boys ranged from 46.7 % to 96.6 % in comparison with non-obese boys. Majority of the obese boys was aged 12 years (+95.3 %) and 16 years (+96.6 %). Obesity of girls ranged from 52.9 % to 88.7 % in comparison with non-obese girls. Majority of the obese girls was aged 10 years (+88.7 %) and 17 years (+84.2 %). Very strong correlation was between body weight and age in non-obese boys (R2=0.9949) and in non-obese girls (R2=0.9378). High correlation was between body weight and age in obese boys (R2=0.875), and in obese girls (R2=0.8533) (Fig. 1).

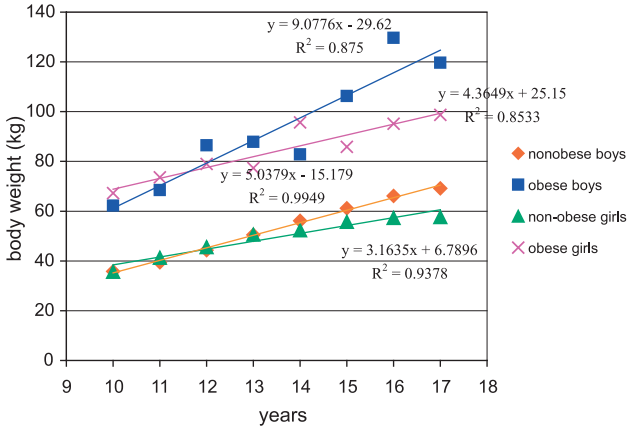


**Fig. 1. Correlation between body weight and age in non-obese and obese children.**

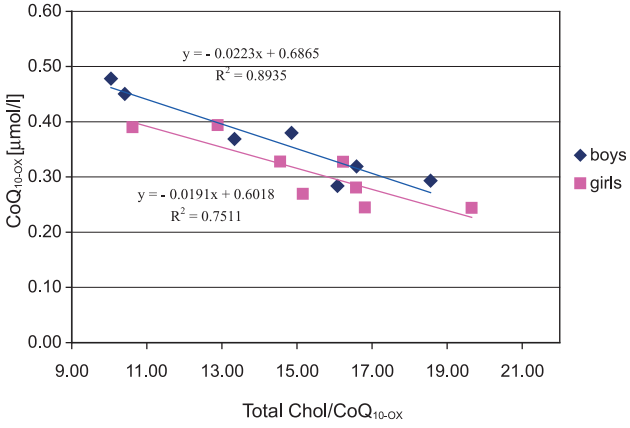


**Fig. 2. Correlation between plasma concentration of $CoQ_{10\text{-}OX}$ and the ratio of total Chol/$CoQ_{10\text{-}OX}$ in plasma of obese children.**

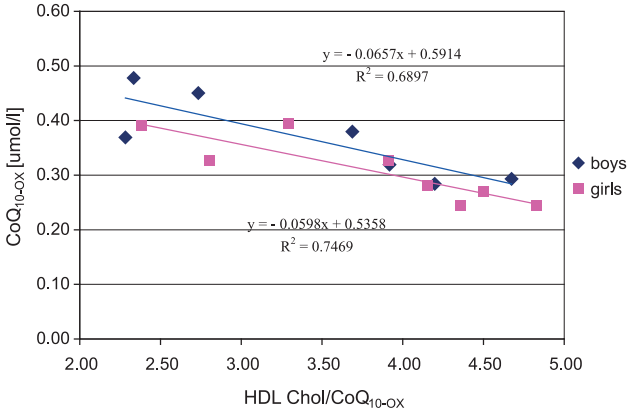


**Fig. 3. Correlation between plasma concentration of $CoQ_{10\text{-}OX}$ and the ratio of HDL Chol/$CoQ_{10\text{-}OX}$ in obese children.**

Table 2 shows significantly decreased $CoQ_{10}$ concentration in obese boys and girls ($p<0.0001$) compared with the non-obese children. α-tocopherol and β-carotene concentrations were in reference values. Malondialdehyde production was significantly increased in obese children ($p<0.0001$) by 44.47 % compared with the control group.

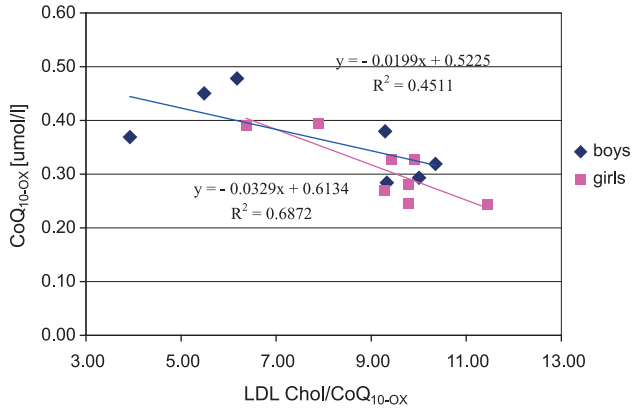


**Fig. 4. Correlation between plasma concentration of $CoQ_{10\text{-}OX}$ and the ratio of LDL Chol/$CoQ_{10\text{-}OX}$ in obese children.**

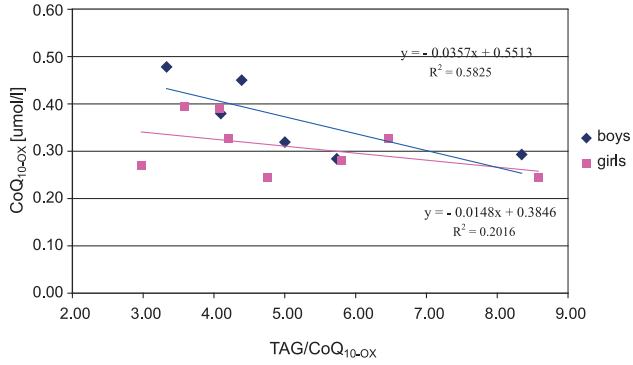


**Fig. 5. Correlation between plasma concentration of $CoQ_{10\text{-}OX}$ and the ratio of TAG/$CoQ_{10\text{-}OX}$ in obese children.**

Table 3 shows that values of LDL-cholesterol and total cholesterol in obese children were within reference values, though significantly higher in obese boys and girls ($p=0.0001$ and $p=0.0296$ respectively) in comparison with the control group. HDL-cholesterol was significantly decreased in obese children (in boys –27.00 %, in girls – 27.7 %, $p<0.001$) and TAG were significantly increased ($p<0.0004$) in obese boys (+67.04 %) and girls (+52.27 %) in comparison with the control group. The ratio of lipid parameters to $CoQ_{10}$ concentration in plasma of obese boys and girls was significantly increased in comparison with the control group: LDL Chol/$CoQ_{10}$ by 147.73 % in obese boys and 176.97 % in obese girls ($p<0.0001$). HDL Chol/$CoQ_{10}$ by 52.73 % in obese boys and by 79.88 % in obese girls ($p<0.0001$), total Chol/$CoQ_{10}$ by 131.04 % in obese boys and 161.55 % in obese girls ($p<0.0001$), TAG/$CoQ_{10}$ by 248.73 % in obese boys and 278.74 % in obese girls ($p<0.0001$) (Tab. 3).

A high correlation was between plasma concentration of $CoQ_{10}$ and the ratio of total Chol/$CoQ_{10\text{-}OX}$ in plasma of obese boys (R2=0.8935) and in obese girls (R2=0.7511) (Fig. 2) as well as between $CoQ_{10\text{-}OX}$ and the ratio of HDL Chol/$CoQ_{10}$ in obese boys (R2=0.6897) and in obese girls (R2=0.7469) (Fig. 3). The

**Tab. 3. Lipid fractions and ratio of lipid fractions to $CoQ_{10}$ in obese and non-obese children.**

| | Reference values | Non-obese children | Obese | |
|---|---|---|---|---|
| | | | Boys | Girls |
| **LDL Chol** [mmol/l] | | | | |
| mean | <3.40 | 2.24 | 2.65 | 2.50 |
| SD | | 0.42 | 0.19 | 0.08 |
| n | | 20 | 49 | 52 |
| P vs Non-obese | | | 0.001 | |
| % vs Non-obese | | **100** | **+18.30** | **+11.61** |
| **HDL Chol** [mmol/l] | | | | |
| mean | >1.16 | 1.37 | 1.00 | 0.99 |
| SD | | 0.21 | 0.04 | 0.04 |
| n | | 20 | 49 | 52 |
| P vs Non-obese | | | <0.001 | |
| % vs Non-obese | | **100** | **-27.00** | **-27.70** |
| **Total Chol** [mmol/l] | | | | |
| mean | | 3.90 | 4.31 | 4.11 |
| SD | <4.8–5.2 | 0.58 | 0.43 | 0.08 |
| n | | 20 | 49 | 52 |
| P vs Non-obese | | | 0.0296 | |
| % vs Non-obese | | **100** | **+10.51** | **+5.38** |
| **TAG** [mmol/l] | | | | |
| mean | <1.3 | 0.88 | 1.47 | 1.34 |
| SD | | 0.43 | 0.11 | 0.30 |
| n | | 20 | 49 | 52 |
| P vs Non-obese | | | <0.0004 | |
| % vs Non-obese | | **100** | **+67.04** | **+52.27** |
| **LDL Chol/$CoQ_{10}$** | | | | |
| mean | | 2.91 | 7.21 | 8.06 |
| SD | | 0.27 | 0.85 | 0.50 |
| n | | 20 | 49 | 52 |
| P vs Non-obese | | | <0.0001 | |
| % vs Non-obese | | **100** | **+147.73** | **+176.97** |
| **HDL Chol/$CoQ_{10}$** | | | | |
| mean | | 1.78 | 2.72 | 3.20 |
| SD | | 0.16 | 0.36 | 0.31 |
| n | | 20 | 49 | 52 |
| P vs Non-obese | | | <0.0001 | |
| % vs Non-obese | | **100** | **+52.73** | **+79.88** |
| **Total Chol/$CoQ_{10}$** | | | | |
| mean | | 5.06 | 11.70 | 13.24 |
| SD | | 0.35 | 1.21 | 0.96 |
| n | | 20 | 49 | 52 |
| P vs Non-obese | | | <0.0001 | |
| % vs Non-obese | | **100** | **+131.04** | **+161.55** |
| **TAG/$CoQ_{10}$** | | | | |
| mean | | 1.14 | 3.99 | 4.33 |
| SD | | 0.27 | 0.72 | 0.65 |
| n | | 20 | 49 | 52 |
| P vs Non-obese | | | <0.0001 | |
| % vs Non-obese | | **100** | **+248.73** | **+278.74** |

lowest correlation was between plasma concentration of $CoQ_{10\text{-}OX}$ and the ratio of LDL Chol/$CoQ_{10}$ in obese boys (R2=0.4511) and obese girls (R2=0.6872) (Fig. 4), and between $CoQ_{10\text{-}OX}$ and the ratio of TAG/$CoQ_{10}$ in obese boys (R2=0.5825) and obese girls (R2=0.2016) (Fig. 5).

## Discussion

Chronic obesity can lead to the development of complications, such as changes in metabolism, impairment of energy metabolism, lipid disorders. Obesity is positively associated with cardiovascular disease risk factors in adolescents and adults. Most of the obese children had at least one cardiometabolic risk factor, particularly lipid disorders (6). The contribution of childhood obesity to the development of adult obesity and subsequent cardiovascular disease was confirmed. Impaired endothelial function, arterial hypertension, subclinical inflammation, and low physical activity are associated with the risk of early atherosclerosis development in obese children (16).

High fat deposition in the organism produces increased free oxygen radicals and oxidative stress (5, 6, 7), which is the key factor in the pathogenesis of metabolic syndrome and may contribute to insulin resistance (8). Table 1 shows overweight of obese children. Most overweight boys were aged 12 and 16 years, girls were aged 10 and 17 years.

Table 2 shows significantly increased malondialdehyde production in obese children compared with the control group. The authors (17) documented the concentration of total $CoQ_{10}$, and ubiquinol, to be similar in children aged 0.2–7.6 years and in adults aged between 29 and 72 years. However, elevated $CoQ_{10}$ and redox ratios (ubiquinol:ubiquinone) do change and could be used as biomarker of oxidative stress in children, while elevated redox ratios in healthy children may be associated with early coronary heart disease development (17).

High concentration of LDL cholesterol, low HDL cholesterol and elevated blood pressure contribute to the development and progression of atherosclerosis [3]. Elevated TAG and low HDL are used as markers of atherogenic dyslipidemia [18]. Other authors did not provide strong evidence that being overweight in childhood would be associated with future CVD risk (19).

In obese children, a significantly higher total cholesterol and LDL-cholesterol was documented in comparison with non-obese children, although these parameters were on the highest reference levels (4). In agreement with these results, Table 3 shows that values of LDL-cholesterol and total cholesterol in obese children were within reference values, though significantly higher in obese boys and girls in comparison with the control group. HDL-cholesterol was significantly decreased and TAG were significantly increased in obese children in comparison with the control group.

Obesity has been associated with lower levels of antioxidants in blood and plasma, which may contribute to a deficient protection of low-density lipoproteins (LDL) against free radicals (3). Lipoproteins, especially LDLs, contain amounts of antioxidants and their oxidative modification is a result of imbalance between oxidative attack and antioxidant mechanisms. LDLs also contain a high concentration of polyunsaturated fatty acids and their oxidation leads to the production of malondialdehyde, a marker of lipid peroxidation. LDLs are easily oxidized and as oxidatively modified LDLs they contribute to the accumulation of lipids, mainly cholesterol and cholesterol esters (20).

It was well documented that hypothalamic centers (paraventricular nucleus and ventromedial hypothalamus) participate in energy homeostasis and in food intake regulation.

Chronic obesity can lead to an impairment of energy metabolism by decreasing the $CoQ_{10}$ concentration in cells. Table 2 shows

that the plasma concentration of $CoQ_{10}$ was significantly decreased in obese children in comparison with the control group. We assume that one of the mechanisms of obesity development could be associated with hypothalamic $CoQ_{10}$ deficiency and decreased hypothalamic function. In contrast to our results, other authors (21) did not find significant differences in coenzyme $Q_{10}$ levels between obese and normal weight children. The concentrations of α-tocopherol and β-carotene were not significantly changed in comparison with the control group. Plasma lipid peroxidation, as parameter of oxidative stress, in obese children was significantly increased ($p<0.0001$) by 44.47 % of control values.

LDL cholesterol and total cholesterol concentrations in obese children were in reference values, but higher in comparison with non-obese children. A high correlation between plasma concentration of $CoQ_{10}$ and the ratio of lipid parameters to $CoQ_{10}$ is associated with child obesity [22].

## Conlusions

An increase of the ratio of lipid parameters to coenzyme $Q_{10}$ is associated with child obesity and could be used as biomarkers for the detection of early complications developing in childhood obesity.

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