INTRODUCTION

The study of lipid profile modifications in children belonging to risk groups is welcome, given the increasing incidence of obesity, atherosclerosis, high blood pressure and type 1 and type 2 diabetes in Romania. Essential prevention must start at birth; the recommended lifestyle must be adequate for the children’s age group and monitoring of any lipid profile modifications must be performed by both the family physician and the paediatrician. Once the risk factors occur, all family members must be carefully monitored by a team of different doctors and by nutritionists in order to prevent the occurrence of complications caused by atherosclerosis.[1–4].

Documented epidemiological studies single out a strong association between a high level of cholesterol and the occurrence of atherosclerosis.[5–7]. Hyperlipidemia has long been acknowledged as a multifactorial condition that involves lifestyle and genetic components.[8]. In both the Muscataine and the Bogalusa Heart Studies, the cholesterol level in childhood proved to be the best predictor of hypercholesterolaemia in adulthood.[9–11].

The American Academy of Pediatrics (AAP) and the Food Commission issued a political declaration in 1998 which encouraged the selective control of children and teenagers with significant family history of coronary disease and/or high values of blood cholesterol in parents.[12,13]. They equally introduced in the study children and teenagers whose family history is impossible to obtain and who suffer from high blood pressure and obesity. The committee predicted that those children would modestly grow up, this depending on their lifestyle. The AAP report published in 2008 admitted that, there may be an additional percentage of 30%–60% of the children with undiagnosed hypercholesterolaemia due to the investigation of a selected control group.[14–17].

The aim of this study was to make a comparative analysis of data from serial measurements of serum cholesterol (TC) level and its fractions: high density lipoprotein (HDL) cholesterol, low density lipoprotein (LDL) cholesterol, very-low density lipoprotein (VLDL) cholesterol, and triglycerides (TG) in patients from the cardiology unit to the data of a control group and to assess the correlations with body weight, body mass index (BMI) and blood pressure. The study cohort included 80 hospitalized patients with CVD and a control group of 84 subjects belonging to groups considered healthy. Patients with dyslipidemia were mainly from urban areas and had a family history of CVD. Significant differences (P < 0.05) were observed between the two groups in terms of the mean values of the lipid profile parameters were normal to high for non-HDL and TC, normal to low for HDL and high for TG. This study suggests that the lipid parameters must be carefully monitored beginning from the age of 2 years to facilitate early diagnosis of any imbalances that cause atherosclerosis and take appropriate preventive measures against related diseases that may arise from an early age.

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(VLDL) cholesterol, non-high-density lipoprotein (non-HDL) cholesterol and triglycerides (TG) in cardiology unit patients to the data of a control group of subjects and to assess the correlations with body weight and body mass index (BMI).

Subjects and methods

This prospective and observational study included a cohort of 80 patients hospitalized in the cardiology section (with hypertension, metabolic syndrome, heart rhythm disorders such as tachycardia, atrioventricular block, Wolff–Parkinson–White syndrome) of ‘Sf. Ion’ Pediatric Emergency Hospital of Galati, between January 2010 and May 2013. Another 84 subjects from non-risk groups (from the general population) took part in the study as a control group. Upon hospitalization, the patients showed clinical signs specific of cardiovascular disease (CVD), and the paraclinical investigations indicated dyslipidemia.

All subjects (via their legal guardians) gave their written informed consent and the study was approved by the local ethics committee at ‘Dunarea de Jos’ University of Galati.

High blood pressure was defined as an increase of systolic and diastolic blood pressure over the 95th percentile for sex, age and height for at least three consecutive measurements through the auscultatory method:

– the normal and high blood pressure is in the range of > 90th percentile and < 95th percentile;
– Stage 1 hypertension: systolic blood pressure and/or diastolic blood pressure between the 95th and 99th percentile + 5 mm Hg;
– Stage 2 hypertension: systolic blood pressure and/or diastolic blood pressure over the 99th percentile + 5 mm Hg.

The statistical analysis was carried out using SPSS 17.0 for Windows, the Kolmogorov–Smirnov test. The normality of the distribution was evaluated using the Kolmogorov–Smirnov, Levene’s test, analysis of variance (ANOVA) and Student’s t distribution for independent and dependent variables. P-values of less than 0.05 were considered to indicate statistically significant differences. Data are presented as mean values with standard deviation (x ± SD).

Results and discussion

The male/female ratio was about 50% in both groups. There were no significant differences between the studied groups (P > 0.05) regarding the average age ranging between 10.9 ± 5.23 years in the group of patients and 9.92 ± 5.06 years in the control group. Noticeably, within the group of patients, there was a slightly higher incidence of patients over 10 years of age suffering from dyslipidemia. Their body weight, BMI, lipid profile and blood pressure were measured and compared to the values of the control group. The reference range values of serum lipid fractions according the National Cholesterol Education Program (NCEP) – Adult Treatment Panel III and AAP are shown in Table 1.

Regarding the area of residence, in the studied group, 67.07% of the patients came from urban areas, and 32.93% from the rural area, which indicates an increased incidence of dyslipidemia and CVD in children from the urban area. The causes behind this phenomenon are most likely hypercaloric food, concentrated sweets, scarce physical activity and smoking, which are more typical of children in the urban areas in Romania. However, there were no statistically significant differences between the mean values of the lipidic profile with respect to the home area (rural/urban).

It was family medical history that was found to be important for the patients hospitalized in the cardiology section. The occurrence of CVD in the family history represents the effect of genetic, biochemical and behavioural components and environmental factors. A positive history of premature coronary disease in a first-degree relative (before the age of 55 years in males or before 65 years in females) is generally considered an important independent risk factor for development of CVD in the

| Lipid profile | Values |
|---------------|--------|
| TC (mg/dL)    | <170: acceptable values |
|               | 170–199: borderline values |
|               | >200: higher values |
| LDL (mg/dL)   | <110: acceptable values |
|               | 110–129: borderline values |
|               | >130: higher values |
| HDL (mg/dL)   | <40: lower values |
|               | 40–45: borderline values |
|               | >45: acceptable values |
| TG (mg/dL)    | 0–9 years of age |
|               | <75: acceptable values |
|               | 75–99: borderline values |
|               | >100: higher values |
|               | >9 years of age |
|               | <90: acceptable values |
|               | 90–129: borderline values |
|               | >130: higher values |
| Non-HDL (mg/dL) | <120: acceptable values |
|               | 120–144: borderline values |
|               | >145: higher values |

Table 1. Reference range values of serum lipid fractions in children and adolescents (NCEP ATP III/ AAP).

Note: Non-HDL cholesterol = TC − (HDL + VLDL), considering Friedewald’s accepted formula, where the VLDL value (mg/dL) = TG/5 (when triglycerides are <400 mg/dL).
The occurrence of atherosclerosis-specific changes is part of a complex process, and the risk is inversely proportional to the age of onset in the parents. Within the age groups of 1–6 years and 6–12 years, there was a homogenous distribution of patients as a function of sex, both in the group of patients and in the control group. However, within the group of patients aged 12–18 years, some difference was observed: the boys with dyslipidemia were prevalent (14.63%) compared to girls (9.76%); however, this difference was not statistically significant. Multiple comparisons of the means of variables analysed in the control group and the group of patients in the cardiology unit are presented in Table 2.

A different distribution of the patients’ weight in the two groups was observed ($P < 0.05$). Since birth, and after the subsequent development in the first stage of childhood, there is a propensity of the child for obesity, insulin resistance and metabolic syndrome, which are favoured by the occurrence of maternal gestational diabetes, small weight at birth and the type of baby feeding in the first year of life. Breastfeeding is recommended for as long as possible (minimum 6 months). If this is not possible, packed maternal milk is recommended, a third option being powdered milk formulas adapted to the baby’s age (those containing polyunsaturated fatty acids are preferred).

According to the World Health Organization classification for children aged 2–19 years, BMI is between the 85th and 95th percentile for overweight children and above the 95th percentile for obese children of the same age and sex. International Diabetes Federation (IDF) recommends primary management in preventing obesity by adopting a healthy lifestyle which includes moderate restriction of calories (in order to lose 5%–10% of the weight in the first year), moderate increase of physical activity and modification of diet. The distribution of patients hospitalized in the cardiology unit depending on BMI was as follows: 35 patients (44%) had normal weight, with BMI below the 85th percentile as a function of age and sex; 18 patients (23%) were overweight, with BMI between the 85th and 95th percentile, and 27 patients (33%) were obese and their BMI was over the 95th percentile.

Measurement of TC and LDL has remained the main goal in the screening of patients with CVD risk factors and in the assessment of the positive effects of the treatment, an aspect which is supported by seriously documented clinical studies [18,19]. The decrease in TC and LDL values is associated with a statistically significant decrease in the mortality caused by CVD. Consequently, their monitoring remains the main goal.

In screening programmes, TC is recommended to be used for estimation of the cardiovascular risk. Nonetheless, high values can be misleading, especially in the case of females who have high HDL and in patients suffering from diabetes mellitus or metabolic syndrome for whom low levels of HDL can often occur. For an adequate analysis of risk factors, HDL and LDL values are dosed in order to be analysed. The evaluation of the total risk does not include patients with family history of hyperlipidemia, who have always run a high risk and are to receive special attention [20–22].

Within the group of patients from the cardiology unit, we observed slightly higher average TC values in the male patients belonging to all age groups, reaching 188 mg/dL for those aged 1–6 years and 6–12 years and 180 mg/dL for the ones aged 12–18 years. In the girls, the average TC values varied between 178 mg/dL and 184 mg/dL. All these are normal to high values. The average values in the control group were within the normal range, except for the group of 6–12-year-olds where we observed an average value of 184 mg/dL, respectively 182 mg/dL (normal to high) for both males and females.

In children, an LDL level below 110 mg/dL is recommended (values ranging between 110 and 130 mg/dL are considered normal to high). Within the group of patients, only in the 12–18-year-olds, the average LDL level in males was 113 mg/dL, which falls within the normal to high range (111 mg/dL for males, respectively 110 mg/dL for females). In the 6–12-year-old boys and girls from the control group, we also observed average values within the normal to high range (111 mg/dL for boys, respectively 110 mg/dL for girls). In the rest of the patients, average values of under 110 mg/dL could be scored.

HDL cholesterol has an important protective role against atherosclerosis through the following mechanisms: it improves the arterial function, diminishes the expression of adhesion molecules, increases the production of nitric acid favouring vasodilation, inhibits

| Parameters          | Control subjects | Cardiology unit patients |
|---------------------|------------------|--------------------------|
| Weight (kg)         | 38.03 ± 20.8*    | 55.04 ± 3.33*            |
| Height (m)          | 1.310 ± 0.27     | 1.39 ± 0.3               |
| BMI                 | 20.51 ± 3.54*    | 25.94 ± 0.83*            |
| Glycemia (mg/dL)    | 86.36 ± 12.82    | 95.05 ± 1.63             |
| VLDL (mg/dL)        | 20.20 ± 14.75    | 29.83 ± 19.84            |
| HDL (mg/dL)         | 50.99 ± 14.27*   | 43.56 ± 1.72*            |
| LDL (mg/dL)         | 88.31 ± 45.40*   | 107.95 ± 3.94*           |
| Total cholesterol (mg/dL) | 159.98 ± 52.19* | 181.69 ± 4.81*           |
| Non-HDL cholesterol | 108.98 ± 49.18*  | 138.12 ± 4.07*           |
| Triglycerides (mg/dL) | 94.52 ± 54.11*   | 165.06 ± 6.62*           |
| Systolic BP (mm Hg) | 105.77 ± 11.27*  | 120.32 ± 1.80*           |
| Diastolic BP (mm Hg)| 63.06 ± 9.88     | 65.86 ± 1.15             |

*Variables whose means are significantly different upon multiple comparison ($P < 0.05$, post-hoc ANOVA, Tukey’s test).
apoptosis in the endothelial cells, diminishes the production of inflammatory cytokines, prevents LDL oxidation and increases the cholesterol flux in the atheroma plaques. The obtained results showed that an increase of 1 mg/dL in the HDL level is associated with a decreased risk of CVD of 2% in men and 3% in women. The Honolulu Heart Study [23] concluded that at any level of TC, the risk of CVD was higher than in the patients suffering from low HDL. In patients suffering from CVD, decompensations are more frequent when the HDL level is under 28 mg/dL and rarer when the HDL level is over 50 mg/dL (CARE trial) [24]. Even ultrasound carotid modifications decrease through therapeutic measures which increase the level of HDL.

Within the group of patients, we found low HDL values in the boys in the 12–18-year-old age group (38 mg/dL) and normal to low values in the girls in the 12–18-year-old age group. For the rest, the other age groups and the control group had normal HDL values.

The TG values are determined using precise, inexpensive enzymatic techniques. A possible error can rarely occur in patients with hyperglycemia, where false high values may be scored. High values can also be scored if associated with low HDL concentrations. Within the group of patients, the analysis of the results showed that the average TG levels were higher than the upper limit of the reference range corresponding to the age, in both the girls and the boys. Thus, the values in the girls were as follows: 166 mg/dL in the 1–6-year-olds, 151 mg/dL in the 6–12-year-olds and 133 mg/dL in the 12–18-year-olds. For the boys between 1 and 6 years old, the TG values reached 124 mg/dL, 205 mg/dL for those 6–12 years old and 188 mg/dL for the ones 12–18 years old.

In the control group, TG had normal values in most of the age groups except for the 6–12-year-old subjects where the mean value was higher than the maximum 100 mg/dL corresponding to the age in both sex groups (110 mg/dL in girls and 109 mg/dL in boys).

Non-HDL cholesterol is used as an estimation of the total number of atherogenic particles in the plasma (VLDL + IDL + LDL) and comprises all the lipid fractions containing apo B. Non-HDL cholesterol can be easily calculated as TC minus HDL cholesterol. In clinical practice, intermediate density lipoprotein (IDL) is included in the LDL measurement and VLDL is calculated using Friedewald’s formula, which considers one fifth of the triglyceride value. Non-HDL cholesterol can offer a better risk estimation in comparison with LDL, especially in case of hypertriglyceridemia in diabetes mellitus, metabolic syndrome or chronic renal disease, which has been reported in a number of recent studies [19,25–28]. It is also useful in monitoring the therapy within these risk groups. In the PDAY 2 study, each increase by 30 mg/dL of the non-HDL cholesterol level was associated with a visible increase of the number of atheroma plaques and of the extension and severity of the atherosclerosis process [21,22].

Within the group of patients, there were statistically insignificantly higher levels of non-HDL cholesterol in boys compared to girls in all age groups, falling within the range of the normal to high values. Thus, the average levels of non-HDL cholesterol reached 140 mg/dL in the boys between 1 and 6 years old and between 12 and 18 years old, and 141 mg/dL in those 6–12 years old, while for the girls, the values reached 136 mg/dL in the 1–6-year-olds, 132 mg/dL in the 6–12-year-olds and 135 mg/dL for those 12–18 years old. In the control group, there were average values within the normal range of HDL cholesterol, except for the age group between 6 and 12 years old, where both the boys (130 mg/dL) and the girls (134 mg/dL) had normal to high values.

Overall, within the studied group, we found that the average values of the lipid-profile parameters were:

- normal for LDL cholesterol (minimum value reaching 34 mg/dL and the maximum one, 201 mg/dL);
- normal to high for non-HDL cholesterol, with an average value of 138 mg/dL, a minimum of 71 mg/dL and a maximum of 231 mg/dL; as well as for TC, which had an average value of 181 mg/dL, with a minimum level of 99 mg/dL and a maximum one of 299 mg/dL;
- normal to low for HDL cholesterol with an average value of 44 mg/dL, a maximum of 79 mg/dL and a minimum one of 12 mg/dL;
- high for TG, which had an average value of 164 mg/dL, with a minimum value of 40 mg/dL and a maximum one of 397 mg/dL.
- There were statistically significant differences ($P < 0.05$) between all these values and the corresponding ones in the control group.

Serial measurements of TG have a prognostic value in the assessment of the risk of coronary disease. Hypertriglyceridemia contributes to the development of atherosclerosis through the atherogenic effect of triglyceride-rich lipoproteins (especially LDL). Equally, hypertriglyceridemia can be associated with other dyslipidemic states, such as decreased HDL cholesterol or increased LDL cholesterol. Moreover, it may disrupt the coagulation mechanism and the fibrinolytic mechanism. In young adults, the serial TG levels have been associated (according to studies on cadavers) to both aortic and coronary lesions and decreased arterial elasticity [29,30].
Conclusions

Although the treatment for arterial high blood pressure is very important, alongside with maintaining normal values of arterial pressure, the results from this study indicate that the lipid profile must be monitored and any imbalances must be corrected so as to slow down the evolution of atherosclerosis, which is known as the silent enemy. The findings from this study showed important lipid disequilibria in the group of patients compared to the control group. Monitoring the biological and medical imaging modifications is not very expensive, and therapy initiation and monitoring must be done in parallel with the treatment of the etiological factors by the practitioner.

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Disclosure statement

No potential conflict of interest was reported by the authors.

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