



Clinical

Pediatric reference data of serum lipids and prevalence of dyslipidemia: Results from a population-based cohort in Germany



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ABSTRACT

Background: Serum lipid concentrations are thought to be risk factors for the development of cardiovascular disease. The present study aims to investigate the prevalence of dyslipidemia and provide sex- and age-related reference values for triglycerides, total cholesterol, LDL and HDL cholesterol as well as apolipoproteins A1 and B by using modern analytical approaches.

Materials and methods: Venous blood and anthropometric data were collected from 2571 subjects of the LIFE Child study, aged between 0.5 and 16 years. Age- and gender-related reference intervals (3rd and 97th percentiles) were established by using Cole's LMS method.

Results: Serum concentrations of TC, LDL-C, TG and ApoB were higher in girls than in boys. In girls TC reached peak levels two years earlier than in boys. Triglyceride levels initially declined until the school age. Until early adolescence there was a steady increase. The LDL-C concentrations in girls and boys followed similar patterns to that of TC. Up to the age of 8 years, a continuous increase in HDL levels for both sexes was found. Due to the strong correlation between HDL-C and ApoA1 ($r = 0.87$) or rather between LDL-C and ApoB ($r = 0.93$), the respective percentiles showed very similar patterns. Dyslipidemia prevalence were as follows: increased TC 7.8%, increased LDL 6.1%, increased TG 0–9 years 22.1%, increased TG 10–16 years 11.7%, and decreased HDL 8.0%.

Conclusion: Age- and sex-related trends for all parameters are similar to those of the German KIGGS study. With the exception of HDL cholesterol, the prevalence of dyslipidemias in the German LIFE Child cohort are similar to the US-American prevalence.

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1. Introduction

There are a lot of studies showing that overweight and obesity correlate with an increased risk for the occurrence of cardiovascular and/or metabolic disease [1]. Unfortunately, some of these mechanisms in children have not been fully understood until now. Heart and circulatory diseases are manifested after the fourth decade of life, whereas the formation of atherosclerosis starts at a distinctly earlier age [2]. The serum lipids are seen as crucial risk factors for the formation of the atherosclerotic disease in later life [3]. Obese children exhibit significantly increased values for TG, TC, LDL, VLDL, and ApoB compared to patients

with normal weight [4]. In addition, a significant correlation between the cholesteryl ester transfer protein (CETP) and pediatric obesity could be established [4]. Normal weight children have in general higher HDL cholesterol levels than obese ones. The concentration of HDL decreases in prepubertal children with progressive weight gain and developmental stage [5]. Moreover, there is a positive relationship between the particle size of LDL and triglycerides. TG are negatively associated with the particle size of HDL [6]. Children with hypercholesterolemia have increased oxidized LDL subfractions and higher concentrations in several inflammatory factors such as tumor necrosis factor related molecules like TNF α . Inflammatory processes are thought to play a role in the development of atherosclerosis [7]. In addition to the clinical laboratory assays of classical serum lipids, there are recommendations to measure apolipoproteins (APO's) [8]. Concentrations of proteins provide additional information about a potential dyslipidemia. Thus, an increased concentration of ApoB, despite normal values of total cholesterol and LDL, is associated with obesity, metabolic syndrome or diabetes, type 2 [8]. The ApoB/ApoA1 ratio is correlated with an increased arterial stiffness in patients with metabolic syndrome, measured by pulse wave

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velocity [9]. The discussion illustrates the central importance of reference values in general and of their clinical interpretation. Age- and gender-related references represent the basis for clinically diagnostic and therapeutic decisions particularly in pediatrics. In recent years, there have been national [10] and international [11] efforts to create expedient reference values for serum lipids. Unfortunately, the apolipoproteins A1 and B were largely excluded. The present study aims to update reference ranges for TG, TC, LDL and HDL cholesterol using modern and current laboratory methods and to determine reference intervals for apolipoproteins A1 and B.

2. Study population and design

The LIFE-Child cohort is a longitudinal study, initiated in July 2011, of the Leipzig Medical Faculty, Department for Child and Adolescent Medicine. The aim of this project is to collect data on growth and development of subjects during the time between birth and adolescence as well as on environmental health determinants [12]. The population, recruited for this study consisted of 2571 children and adolescents of the LIFE-Child Health cohort and the LIFE-Child Obesity cohort aged between 0 and 16 years, in the time between 2011 and August, 2015. A representative cohort for the population of the city of Leipzig and Caucasian/German population was created by the inclusion of the Obesity cohort. There were 1345 boys and 1226 girls included in this analysis. Proband who were treated with lipid-lowering medication were intended to be excluded. However, none of the subjects

fulfilled this criterion. Only healthy subject were included: children with diseases such as diabetes mellitus, inherited metabolic diseases, chromosomal aberrations and chronic kidney and liver disease as well as children with acute illnesses such as bronchitis or otitis media were excluded.

In order to avoid a violation of the independence criteria in the statistical analysis, 75% of families were selected and from these in turn a measured value was used. A weighting procedure was carried out depending on the family size and the number of measured values. So every measurement was drawn with equal probability. For the sample thus obtained reference values were determined. This procedure was repeated 1000 times to determine the average estimated values and their confidence limits. This procedure allows the inclusion of all existing measurement data [13]. Fig. 1 shows the composition of the reference population. Fig. 2 illustrates the age and sex composition of the reference population, with the example of ApoB. To underline the relevance of the newly created reference values for clinical practice, the prevalence of dyslipidemia in the LIFE-Child cohort, as a representative example of Germany, was determined. Therefore, the cut-off values of the S2k guideline [30], which are consistent with the American cut-off values [31], have been taken as a basis.

The study was approved by the Ethical Committee of the University of Leipzig (reference number: Reg. No. 264-10-19042010). LIFE-Child is registered by the trial number: NCT02550236. Participants aged 12 years or older actively consent to every examination, while parents always have to give their written consent in advance.

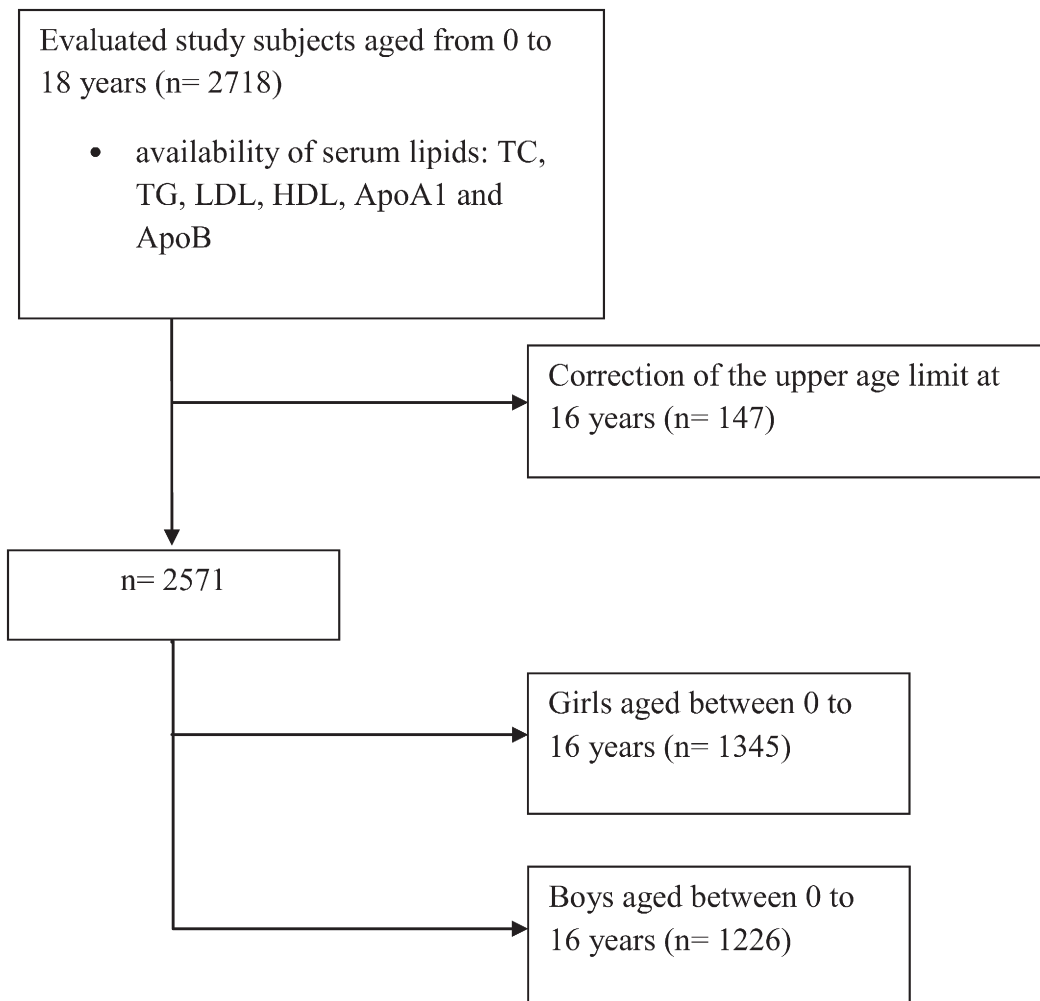


Fig. 1. Composition of the reference population from the LIFE-Child cohort. The flowchart contains information about excluded subjects.

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