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Lipid profiles in a large cohort of Italian children with Down syndrome

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ABSTRACT

Objectives: Results of epidemiological studies of lipid profiles in individuals with Down Syndrome (DS) in different settings showed discordant results but laboratory norms for this population has been lacking. The aim of our study is to evaluate lipid profiles in a large population of Italian children with DS.
Methods: Lipid profiles of 357 patients with diagnosis of DS were recorded. RESULTS: Multiple linear regression was employed to estimate models for each lipid fraction as a function of sex and age in patients with DS.
Conclusions: The main contribution of this paper is to provide data about lipid profile on a large cohort of people with Down syndrome. Long-term surveillance will be crucial to establish if this specific lipid profile may translate into increased morbidity and mortality from cardiovascular diseases (CVD)

1. Introduction

Down syndrome (DS) is the best known chromosomal disorder in humans and the most common cause of intellectual disability, occurring between 1 in 1000 to 1 in 1100 live births worldwide (Irving et al., 2008). Improved medical care during the last 10 years have led to an extraordinary increase of life expectancy with an estimated mean survival approaching the age of 60 years (WHO).

The increased survival has also modified the incidence of chronic conditions such as obesity and insulin resistance, which are now more common among individuals with DS and are associated with unfavorable lipid profiles raising concerns about their long-term health and, in particular, the occurrence of non communicable diseases (NCD) such as atherosclerotic cardiovascular disease (CVD).

In the past, individuals with DS were considered protected from atherosclerotic diseases and in 70's some researchers suggested DS as an "atheroma-free" model of disease (Murdoch et al., 1977).

In the 80's and 90's, results of epidemiological studies in different settings showed that, on the contrary, the risk of mortality from ischemic heart disease and cerebrovascular disease is higher in individuals with DS than in the general population (Englund et al., 2013).

As known, unfavorable lipid profile may be related to increased risk of developing atherosclerotic CVD in the general population and establishing lipid profiles is crucial in order to define preventive strategies.

Indeed, previous studies of lipid profiles in children with DS have produced inconclusive results (Adelekan et al., 2012; Zamorano et al., 1991).

The aim of our study is to evaluate lipid profiles in a large population of Italian children with DS.

2. Materials and methods

All patients with diagnosis of DS consecutively referred to our Hospital over the period December 2013–July 2015 were included in the study.

Anthropometric measurements, comorbidity and family history, focused on Familial Dyslipidemia and/or Early Cardiovascular Disease were collected for each patient.

List of abbreviations: DS, Down Syndrome; CVD, Cardiovascular Disease; NCD, non communicable diseases; TC, total cholesterol; LDL-C, LDL cholesterol; HDL-C, HDL cholesterol; TG, triglycerides.

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Weight and height were converted to age-specific percentiles for DS children by using growth charts (Bull, 2011), according to AAP policy statement for DS children (Zemel et al., 2015). BMI z score was calculated by using age-, race- and gender-specific BMI reference data (Cole et al., 2000).

Since the concentration of serum lipids and lipoproteins increases during early childhood and reaches concentrations similar to adults by approximately 2 years of age (American Academy of Pediatrics, 1992), patients with diagnosis of DS between 2 and 19 years of age were included in the study. A diagnosis of primitive dyslipidemia (familial hypercholesterolemia and hyperchylomicronemia) was considered as an exclusion criteria.

At each well-child visit during the annual follow up, in addition to scheduled blood samples (Cole et al., 2000), each patient was tested for total cholesterol (TC), LDL cholesterol (LDL-C), HDL cholesterol (HDL-C) and triglycerides (TG) after a fast of at least 12 h (ESC/EAS, 2011). For all patients, serum levels of TC, LDL-C, HDL-C and TG were assessed from the same blood sample.

TC, LDL-C, HDL-C and TG levels were analyzed by Enzymatic Assay Kit. (ADVIA Chemistry, Bayer).

The statistical analysis of the results was performed with the program GraphPad Prism 6 software. Unless otherwise indicated, all values were reported as mean or median ± standard deviation (SD) or interquartile range.

Written informed consent from parents and assent from participants were obtained. The study was approved by the ethical committee of the hospital and was conducted in accordance with the principles of the Declaration of Helsinki.

3. Results

One children with DS who was diagnosed with Familial Hypercholesterolemia and was excluded from the study; other children had no anamnestic data suggesting dyslipidemia. A total of 357 children with DS (non-disjunction trisomy 21) met the inclusion criteria.

About 18% of children with DS (34 females, 32 males) were overweight and about 8% (17 females, 15 males) were obese. Descriptive information on study participants are summarized in Table 1.

Multiple linear regression was employed to estimate models for each lipid fraction as a function of sex and age in patients with DS (Table 2) and mean ± standard deviation of lipids levels stratified according to age and sex (Table 3) was reported. Lipid profile in overweight/obese children was summarized in Table 4.

4. Discussion and conclusions

Information on the distribution of lipoproteins in DS group may be important for a variety of epidemiological purposes, and to facilitate diagnosis and treatment of pediatric dyslipidemia. Lipids blood levels were already studied in pediatric patients with DS.

Although these studies all vary significantly in their sample sizes, specific outcomes, and control groups, they nonetheless provide some useful insights into the traditional atherosclerotic risk profiles of the DS pediatric population.

Adelekan et al. (Adelekan et al., 2012) reported that 27 children with DS had less favorable lipid profiles than their siblings, but the results of this study are strongly limited by the small sample sizes.

Zamorano et al. (Zamorano et al., 1991) recorded lipid profiles of 72 children with DS compared with healthy controls and found higher TG, TC, LDL-C, and lower HDL-C levels in DS children.

These results underscore the lack of consensus as to whether lipid profiles of individuals with DS vary from the general population and whether they confer increased atherosclerotic risk.

Mortality from atherosclerotic disease in adults with DS has been studied in previous studies; there are no conclusive population-level data on the incidence of acquired CVD in DS, and no data examining how cardiovascular comorbidities or risk factors in DS might impact on cardiovascular event incidence. Sobey et al. (Sobey et al., 2015) in their recent large-scale study provided estimates of the risk of major cardiovascular events in patients with DS and found that patients with DS were at high risk of cerebrovascular events, but males were at a lower risk of coronary events.

Indeed, laboratory norms for this population has been lacking.

Recently, different academic organizations (Sobey et al., 2015; American Academy of Pediatrics Committee on Nutrition, 2008; Stock and Hayes, 2015) presented guidelines for a more aggressive CVD risk management in pediatric patients. Atherosclerosis is a complex, progressive inflammatory disorder in which dysregulated lipid metabolism plays a central role starting in the pediatric age. High serum TC, in particular high LDL-C level, has been considered the major risk factor for the development of atheromatous plaques and subsequent clinical manifestations like myocardial infarction and stroke (Libby et al., 2011).

Since dyslipidemia is a modifiable risk factor, identification may play a central role in prevention of CVD.

The policy statement from the American Academy of Pediatrics on lipids in childhood (American Academy of Pediatrics Committee on Nutrition, 2008) emphasizes the need to identify dyslipidemic children in order to reduce the risk of adult-onset CVD, offering sex- and age-cut off values for lipid levels.

The AAP percentile cut points are used to identify children and adolescents with abnormal lipid and lipoprotein concentrations, considering “high risk” TC, LDL-C and TG values > 95° centile or HDL-C concentration less than 5° percentile. Comparing values of our population of children with DS, in all ages groups and in both males and females, mean TG, CT and LDL-C levels were >95° percentile, and this remains true also when stratified for BMIz score in overweight and obese children, with the exception of CT levels in girls >15 yrs of age. LDL-C levels were significantly higher in the DS group in all ages and in both male and female, and HDL levels <5° percentile except in girls >15 yrs of age.

It may be argue that estrogen production may play a role in these favorable lipidic status.

Our findings agree with earlier study in adult population (Libby et al., 2011; Draheim et al., 2002; van Gameren-Oosterom et al., 2012) and are consistent with our current understanding of the metabolic syndrome.

In addiction, obesity and diabetes are more frequent in DS children and have to be considered potential comorbidities that increase CVD risk (Sobey et al., 2015). One-third to one-half of children with DS are overweight, and this is true in our population with DS. So, the presence of a less favorable lipid profile may represent an additional risk factor.

Although current health supervision guidelines for children with DS[8] emphasize the importance of preventive interventions in different conditions, there are no specific recommendations

Table 1
Distribution of study participants.

	Subjects with DS
Total[a]	357
Gender, Female[a]	145 (40.6)
Age at visit (years)[b]	7.1 (4.5–11.9)
Overweight[a]	66 (18)
Obesity[a]	32 (8)

[a] Number (percentage).
[b] Median (interquartile range).