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Original Research

Environmental factors, familial aggregation and heritability of total cholesterol, low density lipoprotein-cholesterol and high density lipoprotein-cholesterol in a Brazilian population assisted by the Family Doctor Program

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SUMMARY

Objectives: To estimate familial aggregation and the heritability of total cholesterol (TC), low density lipoprotein-cholesterol (LDL-C) and high density lipoprotein-cholesterol (HDL-C) in families assisted by the Family Doctor Program in a Brazilian city, and to evaluate associations between some environmental factors and familial aggregation of these lipids.
Study design: Cross-sectional familial study.
Methods: The association of lipids with sociodemographic factors, lifestyle factors and comorbidities (e.g. physical activity, alcohol consumption, smoking, hypertension, impaired glucose tolerance, body mass index) was estimated using linear models and generalized estimating equations. Correlation of TC, LDL-C and HDL-C between pairs of relatives was estimated with the familial correlation procedure, and heritability was estimated with the ASSOC procedure.
Results: All associations were statistically significant. There was familial aggregation of TC (parent/offspring, $r = 0.33$; sibling/sibling, $r = 0.37$), LDL-C (parent/offspring, $r = 0.29$; sibling/sibling, $r = 0.37$) and HDL-C (parent/offspring, $r = 0.25$; sibling/sibling, $r = 0.48$), but less than 3%, 6% and 14%, respectively, which was explained by lifestyle factors. Correlation between pairs with genetic sharing (parent/offspring and sibling/sibling) was higher than that observed between father and mother. Heritability estimates ranged between 0.32 (HDL-C) and 0.50 (TC). Similar results were found for the two approaches used to estimate the contribution of genetic and environmental factors in the correlation of TC, LDL-C and HDL-C between the family pairs.
Conclusion: The results showed that there is familial aggregation of TC, LDL-C and HDL-C, and point to the predominance of genetic factors because little influence of environmental variables was found.

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Introduction

High levels of lipids and lipoproteins are recognized risk factors for cardiovascular disease, and represent a major cause of death in developed and developing countries,[1] including Brazil.[2] It has long been recognized that the levels of total cholesterol (TC), high density lipoprotein-cholesterol (HDL-C) and low density lipoprotein-cholesterol (LDL-C) aggregate within families.[3] In a review of twin studies, the genetic inheritance of the lipid profile varied widely, from 22% to 98%, with a tendency to be higher among younger individuals.[4] Lifestyle variables, including alcohol consumption, exercise and dietary factors, are known to relate to TC, HDL-C and LDL-C. To the authors' knowledge, only one study has examined the relationship between lifestyle factors and the determinants of familial aggregation, concluding that lifestyle factors make little contribution to the familial aggregation of lipoproteins.[3] Investigation of the contribution of familial aggregation and environmental factors can help to identify risk groups and guide interventions aimed at preventing the development of cardiovascular disease.[5]

The Family Doctor Program (FDP) of Niterói, Rio de Janeiro, Brazil is a public primary healthcare programme targeted at the underprivileged (approximately 25% of the total population of the municipality). In each geographic area, a general practitioner and a nursing assistant that live in the community are responsible for the care of 250 families (average 1200 people). The programme adopts an approach based on health promotion; families are registered and the targeted population is monitored regularly.[6]

The aim of this study was to estimate familial aggregation and the heritability of TC, LDL-C and HDL-C in families assisted by the FDP in a Brazilian city, and to evaluate associations between some environmental factors and familial aggregation of these lipids.

Methods

The study used data from participants in the CAMELIA study, which was conducted between June 2006 and December 2007. In total, 1098 subjects were recruited from the FDP. Thirteen FDP units were selected by convenience to cover all administrative areas of Niteroi city. In 2005, the FDP had 29 units; in some areas, there was just one unit. Families were enrolled following initial selection of probands. To be accepted as a proband, the subject had to be married to a partner who agreed to participate in the study and had to have at least one child between the ages of 12 and 30 years who would also be enrolled in the study. Four groups of probands were recruited: (1) hypertensive patients without diabetes; (2) diabetic patients with hypertension; (3) diabetic patients without hypertension; and (4) patients without either hypertension or diabetes. Probands were selected at random from the subjects who met the inclusion criteria. Pregnant women and those with immunodeficiency or on immunosuppressive agents (steroids and/or cytostatic drugs) were excluded.

After the pilot project, trained researchers visited the FDP facility in each community. The participants answered a questionnaire that contained items related to comorbidities and demographic, socio-economic and lifestyle factors. Medical staff collected personal and family medical history. Blood pressure was measured, and blood and urine samples were collected. Nutritionists assessed anthropometric and nutritional status. Weight was measured with a digital balance scale (S/A, Model PL18, Brazil) with a weight limit of 150 kg and an accuracy of 0.1 kg, and height was measured with a digital stadiometer (Kirchnner Wilhelm Medizintechnik, Germany) with an accuracy of 1.0 cm. Blood pressure was measured using an electronic sphygmomanometer (Hem-711AC, Omron Co., Japan). Three measurements were taken, and the mean of the second and third measurement was considered. When the difference between two measurements was greater than 5 mmHg, an additional measurement was taken to replace one of the measurements. Biochemical analyses were accomplished using a chemistry analyser (Selectra, Vital Scientific NE, Netherlands).

All individuals with complete survey data were considered for this study. Per-capita monthly income was classified into three categories: ≤US$100.00, >US$100.00–200.00 and >US$200.00. The minimum wage per month in Rio de Janeiro State was approximately US$200.00. Education was classified into two strata: 'never studied or studied until fourth grade' and 'studied beyond fourth grade'. As the minimum age for participation in the study was 12 years, it was considered that not having studied beyond fourth grade meant exposure to risk. Skin colour was classified as black, brown or white. Participants completed a questionnaire on leisure-time physical activity, which contained questions about physical activities performed in the last 15 days, details of the activities, the number of times practised per week, and the time spent at each activity.[7] Those who reported <150 min of physical activity during leisure time[8,9] were considered sedentary. Participants were classified as non-smokers, ex-smokers or current smokers. Food consumption was estimated using two different food frequency questionnaires, one specific for adolescents[10] and one for adults.[11] To calculate the participants' daily intake of food portions, the frequency was converted to daily values. The values of daily attendance multiplied by the serving of each item consumed equalled the number of servings consumed daily from each food group. Food groups were proposed by Nettleton *et al.*[12] and adjusted by nutritionists who worked on the research project. Individuals were classified as hypertensive if they had previously been diagnosed as such, or if they had systolic blood pressure >140 mmHg and diastolic pressure >90 mmHg. Body mass index (BMI) was calculated as body weight (in kg) divided by squared height (in m). Glucose impairment was considered if fasting serum glucose was ≥100 mg/dl (impaired glucose tolerance or diabetes). TC, LDL-C, HDL-C and BMI were analysed as continuous variables.

Statistical analysis

The association between lipids and sociodemographic factors, lifestyle factors and comorbidities was investigated. Variables without a normal distribution (TC, LDL-C, HDL-C and BMI) were log transformed. All variables associated with TC, LDL-C and HDL-C with a significance level of 0.05 in unadjusted models were included sequentially in the following three models: