Clinical research

Risk factor indicators in offspring of patients with premature coronary heart disease in Banja Luka region/Republic of Srpska/Bosnia and Herzegovina

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Abstract

Introduction: Risk factor differences among offspring of patients with premature coronary heart disease (CHD) have not been widely studied.

Material and methods: We examined 161 persons from the region of Banja Luka, including 81 children (mean age: 25.9 years, 45.7% female) with a history of CHD and a control group of 80 persons (mean age: 24.1, 50% female). Medical history interviews and risk factor measurements were performed.

Results: There were differences in mean body mass index (BMI) (26.1 kg/m² vs. 23.1 kg/m², p < 0.0001), waist circumference (87.7 cm vs. 83.9 cm, p = 0.002), hip circumference (99.3 cm vs. 95.8 cm, p < 0.002), systolic blood pressure (BP) (128.09 mm Hg vs. 122.7 mm Hg, p = 0.007), and diastolic BP (99.3 mm Hg vs. 95.8 mm Hg, p = 0.07). Moreover, HDL-cholesterol was significantly lower (1.1 mmol/l vs. 1.4 mmol/l, p = 0.0001), triglycerides significantly higher (2.2 mmol/l vs. 1.6 mmol/l, p = 0.001), and TC/HDL-ratio was significantly higher (5.1 vs. 4.0, p < 0.001) comparing cases and controls, respectively, adjusted for age, gender, and standard CHD risk factors total cholesterol, LDL and HDL cholesterol, smoking, systolic and diastolic BP, and BMI, those with HDL-C > 1.0 mmol/l in men and 1.2 mmol/l in women had a reduced odds (OR = 0.08, 95% CI: 0.02–0.34 of CHD as well as those with change of fat type (OR = 0.26, 95% CI: 0.11–0.60).

Conclusions: Children of parents with premature CHD have a significantly greater burden of CHD risk factors, with low HDL-C, in particular, being associated with an increased likelihood of being a child of a parent with premature CHD.

Key words: lipids, family history, coronary heart disease, children.

Introduction

In the past five decades, considerable evidence has supported the contention that atherosclerosis may begin early in life and progress, especially in children of parents with coronary heart disease (CHD) [1, 2]. It has become clear that both genetic and environmental factors are implicated in the pathogenesis of atherosclerosis and subsequent CHD [3, 4]. The most important goals for primary prevention are to identify and develop interventions to lower risk factors of CHD risk.
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during childhood and adolescence [5–9]. Guidelines on the prevention of cardiovascular disease recommend screening in close relatives of patients with premature CHD [10, 11]. Many of them also have modifiable risk factors. Children of parents who had CHD had significantly higher levels of total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), glucose, and body weight as compared to those without a parental history. Risk factor control and lifestyle changes are the foundation of primary prevention efforts. Studies of preventive measures in close relatives of CHD patients show high prevalence of bad lifestyle characteristics and risk factors, including national multicenter studies such as EUROASPIRE II (1999/2000) [12, 13]. Using a postal questionnaire EUROASPIRE II determined in the families (first degree blood relatives) of patients with premature coronary heart disease (men under age 55 years and women under age 65 years at time of first event) whether screening for risk factors has occurred and, if so, their management by lifestyle and drug therapies. With similar methodology we assessed the extent of CHD risk factor control, goal attainment, adherence to recommended treatments, and risk factors in young adults who had parents with premature CHD in the Banja Luka region of the Republic of Srpska, Bosnia and Herzegovina.

Material and methods

We examined 161 young adults aged 18 to 32 years from the region of Banja Luka, Bosnia and Herzegovina, including 81 young adults with a premature family history of myocardial infarction (defined as one or more first degree male relatives who experienced CHD before age 55 or first degree female relatives who experienced CHD before age 65), and a control group of 80 persons matched by age and gender free of a family history of myocardial infarction (no CHD before age 55 in a first degree female or before age 65 in a first degree male relative) from the same clinic. The participants gave written informed consent, and the study was approved by the local ethics committee.

Measurements

Medical history interviews and risk factor measurements were performed with lipid levels assessed by the Cholestech LDX analyzer using reflectance photometry. Blood pressure was measured using a mercury sphygmomanometer, and the mean of 2 readings was taken. Total cholesterol and triglycerides were measured enzymatically. HDL cholesterol (HDL-C) was measured directly in the serum, and LDL-C levels were calculated using the Friedewald formula. Body height (in cm) was measured without shoes, with the heels placed together. Body weight (in kg) was measured on the medical digital scale in minimal underwear. Waist circumference was measured with a metal tape measure. Body mass index (BMI) was calculated as weight (kg)/height (m²). The following parameters were measured: fasting glucose, total cholesterol, triglycerides, HDL cholesterol (HDL-C), proportion at HDL-C goal, TC/HDL ratio, systolic and diastolic blood pressure, LDL cholesterol (LDL-C), glucose, and body weight. The participants were asked whether they had made the noted change before seeing health professionals, within the period from 1 to 5 years prior to the clinic visit.

Statistical analysis

The χ² test of proportions for categorical variables or Student's t-test for continuous variables was used to compare children with a parental history of CHD to the control group without. We also used multiple logistic regression (providing odds ratios and 95% confidence intervals), adjusted for other risk factors, to examine variables independently associated with being a case child with a parental history of CHD. All analyses were performed with SPSS/Windows statistical software.

Results

There were 81 young adults (mean age: 25.9 years, 45.7% female) with a premature family history of myocardial infarction and 80 (mean age: 24.1 years, 50.1% female) in the control group without a parental history of myocardial infarction. The two groups were compared in order to compare risk factors in those with versus without a premature family history of CHD.

Comparison of demographic and health behavior characteristics showed a difference in age, living environment (apartment or house), number of cigarettes smoked daily, and health nutrition (fat intake reduction, reduction of calories, and blood pressure. Young adults with a premature family history of CHD had increased risk factors including elevated systolic and diastolic blood pressure, elevated glucose, and cholesterol (Table I). When parameters were measured after the interview, it was found that there was a difference in BMI, waist circumference, hip circumference, waist-to-hip circumference ratio, systolic and diastolic blood pressure, HDL-C, proportion at HDL-C goal, TC/HDL ratio.
ratio, triglycerides and proportion at triglycerides goal (Table II). Comparing children from parents with CHD versus the control group, there were differences in mean BMI (26.1 kg/m² vs. 23.1 kg/m², \( p < 0.0001 \)), waist circumference (87.7 cm vs. 83.9 cm, \( p = 0.002 \)), hip circumference (99.3 cm vs. 95.8 cm, \( p < 0.002 \)) systolic blood pressure (128.1 mm Hg vs. 122.7 mm Hg, \( p = 0.007 \)), diastolic blood pressure (99.3 mm Hg vs. 95.8 mm Hg, \( p = 0.07 \)), and the proportion achieving the target value of systolic blood pressure (22% vs. 10%, \( p < 0.016 \)). Moreover, HDL-C was significantly lower (1.1 mmol/l vs. 1.4 mmol/l, \( p = 0.0001 \)), the proportion achieving the target value of HDL-C was significantly lower (44% vs. 61%, \( p < 0.003 \)), triglycerides were significantly higher (2.2 mmol/l vs. 1.6 mmol/l, \( p = 0.001 \)), the TC/HDL ratio was significantly higher (5.1 vs. 4.0, \( p < 0.001 \)), and the proportion achieving the target value of triglycerides was also greater (50% vs. 35%, \( p < 0.017 \)), comparing cases and controls, respectively.

Analysis using univariate logistic regression showed that the odds of being a child with a premature family history of CHD were associated with age, marital status, physical activity, nutrition (taking a certain type of fat, reduction of calories, Table I. Demographic and lifestyle variables in offspring of parents with CHD and controls (descriptive statistics – frequencies, means and SDs; and univariable logistic regression – ORs with 95% CIs)

| Parameter                                                                 | Offspring of CHD (n = 81) | Control group (n = 80) | OR 95% CI |
|---------------------------------------------------------------------------|---------------------------|------------------------|-----------|
| **Demographics:**                                                        |                           |                        |           |
| Age [years]                                                               | 25.9 ±5.1*                | 24.1 ±5.3              | 1.07*     | 1.01–1.14 |
| Sex (male/female)                                                         | 54.3/45.7                 | 50.0/50.0              | 0.84      | 0.45–1.56 |
| Married (yes/no)                                                          | 42.0                      | 25.0                   | 2.17*     | 1.10–4.24 |
| Social status (domestic/refugee)                                          | 74.1/25.9                 | 76.3/23.8              | 0.88      | 0.43–1.82 |
| Work status (employed/unemployed including pensioners)                    | 44.4/55.6                 | 33.8/66.3              | 1.57      | 0.82–2.97 |
| Education level (elementary school/high school or faculty)                | 14.8/85.2                 | 5.0/72.5               | 0.89      | 0.62–1.29 |
| Living environment (apartment or house/other)                             | 86.4/13.6*                | 72.5/27.5              | 1.53*     | 1.03–2.28 |
| Income (bad/satisfactory-good)                                           | 90.1/9.9                  | 85.0/15.0              | 1.32      | 0.84–2.08 |
| Stress (occasional-permanent/no stress)                                   | 43.2/56.8                 | 46.3/53.8              | 0.87      | 0.57–1.34 |
| **Lifestyle factors:**                                                     |                           |                        |           |
| Smoking status (current or ex-smoker/non-smoker)                           | 45.7                      | 31.3                   | 1.34      | 0.96–1.86 |
| Duration of smoking [years]                                               | 10.2 ±5.8                 | 10.4 ±5.1              | 1.00      | 0.91–1.10 |
| Number of cigarettes                                                      | 20.3 ±5.5*                | 22.2 ±8.6              | 0.96      | 0.89–1.04 |
| Advice for smoking cessation if smoker (yes/no)                           | 56.8                      | 48.0                   | 1.42      | 0.51–3.93 |
| Tried to quit smoking if smoker (yes/no)                                  | 56.8                      | 24.0                   | 1.71      | 0.54–5.35 |
| Alcohol use (yes/no)                                                      | 69.1                      | 73.8                   | 0.78      | 0.40–1.58 |
| Talk about physical activity with health worker (yes/no)                  | 69.1                      | 76.3                   | 0.82      | 0.43–1.54 |
| **Lifestyle changes (before seeing health professionals):**               |                           |                        |           |
| Salt reduction (yes/no)                                                   | 19.8                      | 37.5                   | 0.41*     | 0.20–0.83 |
| Fat reduction (yes/no)                                                    | 19.8                      | 32.5                   | 0.51      | 0.25–1.05 |
| Change of fat type (yes/no)                                               | 18.5*                     | 48.8                   | 0.24**    | 0.12–0.49 |
| Calorie intake reduction (yes/no)                                         | 19.8*                     | 43.8                   | 0.32**    | 0.16–0.64 |
| Eating more fruits and vegetables (< 5 times per day vs. ≥ 5 times per day)| 19.8                      | 32.5                   | 0.51      | 0.25–1.05 |
| Eating more fish (< 2 times per week vs. ≥ 2 times per week)             | 19.8*                     | 45.0                   | 0.30**    | 0.15–0.61 |
| Weight loss                                                               | 17.3                      | 30.0                   | 0.49      | 0.23–1.03 |

Variables (mean ± SD or %). *\( p < 0.05 \); **\( p < 0.01 \) when compared to reference.
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Table II. Risk factors (descriptive statistics – frequencies, means and SDs; and univariable logistic regression – ORs with 95% CIs)

| Risk factors                           | Children (n = 81) | Control group (n = 80) | OR    | 95% CI       |
|---------------------------------------|------------------|------------------------|-------|--------------|
| BMI [kg/m²]                           | 26.1 ±3.9**      | 23.2 ±2.7              | 1.30**| 1.17–1.44    |
| Waist circumference [cm]              | 87.7 ±8.2**      | 83.9 ±7.5              | 1.07**| 1.02–1.11    |
| Hip circumference [cm]                | 99.3 ±8.0**      | 95.8 ±7.1              | 1.06**| 1.02–1.11    |
| Systolic blood pressure [mm Hg]       | 128.1 ±13.2**    | 122.8 ±11.6            | 1.04**| 1.01–1.06    |
| Target value of systolic blood pressure (< 140 mm Hg) | 72.8*             | 87.5                   | 2.60* | 1.14–5.94    |
| Diastolic blood pressure [mm Hg]      | 82.4 ±8.4        | 80.1 ±7.1              | 1.04  | 0.99–1.08    |
| Target value of diastolic blood pressure (< 80 mm Hg) | 72.8              | 80.0                   | 1.58  | 0.76–3.29    |
| Total cholesterol [mmol/l]            | 5.1 ±1.0         | 5.1 ±0.8               | 0.99  | 0.69–1.40    |
| Target value of total cholesterol (< 5 mmol/l) | 49.4             | 47.5                   | 0.92  | 0.49–1.72    |
| HDL-C [mmol/l]                        | 1.1 ±0.2**       | 1.4 ±0.4               | 0.04**| 0.01–0.14    |
| Target value of HDL-C (> 1.0 mmol/l in men; > 1.2 mmol/l in women) | 54.3              | 76.3                   | 1.48**| 1.20–1.82    |
| Non-HDL-C [mmol/l]                    | 4.0 ±1.1         | 3.7 ±1.0               | 1.30  | 0.96–1.76    |
| LDL-C [mmol/l]                        | 3.2 ±0.9         | 3.0 ±0.9               | 1.24  | 0.88–1.75    |
| Target value of LDL-C (< 3 mmol/l)    | 38.3             | 51.3                   | 1.70  | 0.91–3.17    |
| Triglycerides [mmol/l]                | 2.2 ±1.2**       | 1.6 ±1.0               | 1.69**| 1.21–2.36    |
| Target value of triglycerides (< 1.7 mmol/l) | 38.3*             | 56.3                   | 2.07* | 1.10–3.89    |
| Glucose in blood [mmol/l]             | 5.3 ±0.9         | 5.1 ±0.8               | 1.20  | 0.83–1.73    |

Table III. Multivariable regression of indicators of child with parental history of CHD

| Models | Variables | Final model |
|--------|-----------|-------------|
|        | MOR       | 95% CI      |
| Age    | 25.9 ±5.1 | 1.07        |
| Gender (M/F) | 54.3/45.7 | 0.84        |
| Smoking status | 45.7        | 1.34        |
| Systolic blood pressure | 128.1 ±13.2 | 1.04        |
| Diastolic blood pressure | 82.4 ±8.4 | 1.04        |
| BMI [kg/m²] | 26.1 ±3.9 | 1.28        |
| HDL-C [mmol/l] | 1.1 ±0.2 | 0.08        |
| Demographics | Married (yes, no) | 2.17 | 1.10–4.24 |
| Living environment (apartment or house) | 2.00 | 1.20–3.33 |
| Lifestyle changes (before seeing health professionals) | Change of fat type (yes, no) | 0.26 | 0.11–0.60 |

Taking more fish, counseling for elevated blood pressure, systolic and diastolic blood pressure level, cholesterol, BMI, waist circumference, hip circumference, HDL, proportion achieving HDL goal value, triglycerides and proportion achieving triglycerides goal value. Adjustment for age, gender, total cholesterol, LDL and HDL cholesterol, smoking, systolic and diastolic BP and BMI showed that lower odds of having a parent with a premature family history of CHD were noted in those who...
changed fat type (OR = 0.26, 95% CI: 0.11–0.60) and those who had higher HDL-C (OR = 0.08, 95% CI: 0.02–0.34) (Table III).

Discussion

Our study showed that young adults with a parental history of CHD have higher BMI, waist circumference, hip circumference, waist-to-hip circumference ratio, systolic and diastolic blood pressure, triglycerides, and TC/HDL ratio, and lower HDL-C (> 1.0 mmol/l in men; > 1.2 mmol/l in women) compared to controls without a parental history of CHD. The results were compared to those in the EUROASPIRE II study, where the children of patients showed a high prevalence of elevated risk factors and insufficient use of measures for primary prevention [12, 13]. Analysis of risk factors showed that 45.6% were smokers, which can be compared with 48.3% in the EUROASPIRE II study. In our study, 14.8% of patients had high blood pressure, compared to 8.3% in the EUROASPIRE II study, and high cholesterol was present in 12.3% and 19.6%, respectively. 12.3% were obese in our study, compared to 15.3% in EUROASPIRE; 60.4% were at least overweight (with BMI ≥ 25 kg/m²), compared to EUROASPIRE II with 46.6%. When examining the prevalence of preventive measures, 19.7% of children of parents with CHD showed decreased fat intake compared to 21.7% in EUROASPIRE II. Salt intake was reduced in 19.7% of our children of parents with CHD, compared to 13.9% in EUROASPIRE II. The consumption of more fruits and vegetables (≥ 5 times per day) was present in 19.7% and 23%, respectively, and losing weight was noted in 18.5% and 21%, respectively. Physical activity, however, was much more prevalent in our study (87%) compared to EUROASPIRE II (27.9%). Results showed that preventive measures were uncommon, especially for healthy nutrition habits, which are also lacking in other European countries. There must be more emphasis on the necessity of physical activity in children in our study, which was different than in other European countries.

In the Coronary Artery Risk Development in Young Adults (CARDIA) prospective study of African-American and Caucasian women and men aged 18 to 30 at baseline, parental risk indicators were consistently associated with increased CHD risk in their offspring. Subjects with a parental history of myocardial infarction had higher levels of total cholesterol and blood pressure and lower levels of HDL-C [14]. In the Bogalusa Heart Study, children of parents who had experienced myocardial infarction or who were diabetic had significantly higher levels of total cholesterol, LDL-C, insulin, glucose and body weight as compared with those without a parental history [15].

The issue of lipid levels of offspring with or without a family history of premature CHD was investigated two decades ago [16–19]. Widhalm et al. examined serum lipids, lipo- and apolipoproteins in 338 offspring whose fathers and/or mothers had been affected with a myocardial infarction before the age of 55, in comparison with 448 age- and sex-matched, healthy controls, and found HDL-C to be lower, and the ratios of total cholesterol and LDL-C to HDL-C to be higher, comparing children of affected vs. non-affected parents [20].

Our case-control study has several strengths and limitations. While we had standardized procedures for measurement of risk factors and evaluations of medical history, not all participants had risk factor measurements available; hence estimates could be biased if those with missing information on risk factors were not representative of the whole cohort. A strength of the study is the standardized assessment of risk factors and medical history/lifestyle information by questionnaire. A larger sample size would have been desirable for the study in order to detect more subtle differences between cases and controls. The rest of the risk factor differences could be explained by other hereditary or environmental factors such as growing up in the same home in the same community. Parents are often the role models of their children.

Children of parents with premature CHD have a significantly greater burden of CHD risk factors. Low HDL-C, in particular, is independently associated with the odds of being a child of a parent with premature CHD. This emphasizes the need for greater attention to be paid to primary prevention efforts to control risk factors in children of CHD patients.

Conflict of interest

The authors declare no conflict of interest.

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