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EVALUATION OF CARDIOVASCULAR RISK FACTORS IN CHILDREN – 15 YEARS OF PROSPECTIVE YUSAD STUDY

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Abstract

Atherosclerosis is dynamic process of cholesterol accumulation and other fatty substances in the artery wall over individual's lifetime, leading to the reduction in hemodynamics of blood vessels and atherothrombosis. Yugoslav Study of Atherosclerosis precursors in School Children (YUSAD) presents prospective longitudinal study that included so far 3 examinations on same school children population. First examination was done in 1998 in 15 cohorts including cohorts from Serbia, Bosnia and Herzegovina, Montenegro and Greece, when children were 10 years of age, where the main research is focused on risk factors for atherosclerosis development in school children and youth. The evaluated population was screened every 5 years. On first and second examination there were 4208 participants, 2124 males and 2084 females. On third examination there were 1293 participants, composing of 555 males and 738 females. The YUSAD study is designed through 7 chapters: epidemiological, clinical, anthropometric, biochemical, nutrition, genetics and ECG. Our study demonstrated that majority of tested school children were normotensive for age and gender, close to the half of evaluated population. Further, we have demonstrated that girls are more prone to accumulate body fat versus boys in the YUSAD study. Frequency of metabolic syndrome in school children population included in the YUSAD study was less than frequency reported in the literature. There is increase in mean values of total cholesterol and LDL fractions from E2 to E4 genotype in evaluated population. Triglycerides levels differ in mean values in different apo-E genotypes. School children from YUSAD study are physically active in moderate range, with preference given to those from rural places.

Keywords: Atherosclerosis; Risk factors; YUSAD study; Children

Introduction

Atherosclerosis is dynamic process of cholesterol accumulation and other fatty substances in the artery wall over individual's entire lifetime, leading to the reduction in hemodynamics of blood vessels and to atherothrombosis. According to the pathobiologic findings, atherosclerosis begins in early life and continues to its final stages in later life. The main characteristic of this process is long silent period. Significant reduction of the lumen during the years may lead to the critical reduction of blood flow in the affected part of vessel lumen resulting in ischemic events (1.2). There is increased frequency of atherosclerosis risk factors, particularly reduction in physical activity and obesity worldwide both in developed and developing countries, stressing out necessity of bringing the well developed and accessible educational programs that could be easily implemented.

Yugoslav Study of Atherosclerosis Precursors in School Children (YUSAD) represents a prospective-longitudinal study, where the main research is focused on risk factors for atherosclerosis development in school children and youth (1.2).

YUSAD is one of the largest national studies in Serbia with international character since it included cohorts from Serbia, Montenegro, Bosnia and Herzegovina and Greece as well.

So far, among many, few risk factors for development of atherosclerosis include: obesity in children (obesity), physical inactivity, genetic factors, metabolic syndrome, diabetes mellitus type 2, hypertension, smoking, hyperlipidemia, smoking, stress, risky behaviour in youth, etc. (2).

Study aims

The most important aims of the YUSAD study are (1.2):

1. Evaluation of selected parameters in school children
1. Identification of atherosclerosis precursors in school children population
2. Identification of children at mild, moderate and high risk
3. Estimation of prevalence and incidence of morbidity and mortality in parents and children through long term follow-up

Study material and methods

The YUSAD study as prospective longitudinal study included 3 examination periods performed on a same population. The first examination was done in 1998 in 15 cohorts including cohorts from Serbia, Bosnia and Herzegovina, Montenegro and Greece. The second examination that was conducted in 2003also included 15 cohorts, while the third check-up that was done in 2007 consisted of population from 9 cohorts from Serbia. The age of participants was 10 years on first examination, 15 years on second and 19/20 years on third. The evaluated population was screened every 5 years.

The study was approved by Institutional Review Board of Medical School University of Belgrade and supported by most prominent institutions in Serbia. International Commission in Bologna recognized YUSAD as a project of national interest. Prior to inclusion of eligible participants in the study, parents or legal guardians were informed and consent was obtained.

On first and second examination there were 4208 participants, of which 2124 were males and 2084 females (1). On third examination there were 1293 participants, composing of 555 males and 738 females (2).

The YUSAD study is designed through 7 chapters: epidemiological (65 characteristics), clinical (68 characteristics), anthropometric (14 characteristics), biochemical (17 characteristics), nutrition (19 characteristics), genetics (19 characteristics) and ECG (24 characteristics) (1). The most significant anthropometric parameters included: body mass index (BMI), waist circumference (Wc), hip circumference (Hc), skin fold on arm (SF), subscapular skin fold (SuS) and upper arm circumference (UAc). Anthropometric parameters were analyzed in the morning before meal in light clothes. Cardiovascular parameters included among others: blood pressure (systolic and diastolic), heart rate (pulse) and ECG evaluation. The cut-off values for blood pressure were 90^{th} and 95^{th} percentile for gender, age and height. The genetic parameters: MTHFR and apo-E genotypes.

Study findings of selective parameters

Cardiovascular parameters (2–4):

From the evaluated school children population, over the period of 15 years, we have found that there is less than 1% of those with congenital heart defects, acquired heart defects and/or myocardial and/or pericardial diseases.

There is increase in both systolic and diastolic blood pressure over 15 years of follow-up in evaluated population, but such increase is in correlation with normal physiological development and growth. Our study also demonstrated that majority of school children were normotensive for age and gender, close to the half of evaluated population.

Further, we have demonstrated that changes in diastolic blood pressure are more closely associated with gender and age of participants, contrary to the findings regarding the systolic blood pressure between the age of 10 and 15 years. Furthermore, it is pointed out that diastolic prehypertensive state is more likely to be noticed in younger school children while diastolic hypertensive state is more likely to be found in older school children from evaluated population.

Anthropometric parameters (2.5):

Over the period between 10 and 15 years of age in the group of boys it is noticed that there is significant increase in mean values of evaluated anthropometric parameters (BMI, Wc, Hc, SuS and UAc), while there were no significant changes in the mean values of SF. Significant increase for all parameters was noticed over the 10 years period in the group of boys. Regarding the group of girls, we found same trends over the same periods for same evaluated parameters. When such parameters were compared between genders it was shown that significant differences persist for every parameter except for pelvic diameter on all 3 examinations and UAc for the group of 10 years of age. In the YUSAD study we have demonstrated that girls are more prone to accumulate body fat versus boys. The possible explanation for such claims could be found in reduced physical activity for the female population. Furthermore, it was shown that there is different proportion of overweight and obese children in different centres from YUSAD study. This could lead to the necessity of introduction of preventive and educational programs in whole society for early detection of risk factors and implementation of healthy dietary habits and proper regular physical activity. In YUSAD study, as well as in other studies, we have noticed that risk for cardiovascular disease curve tends to have "J" distribution.

Lipid parameters (2.6):

Result from our study demonstrated that there are significant changes in lipid fractions: total cholesterol, triglycerides and LDL in boys population, while we found no significant change in mean values of HDL over 15 years of follow-up / concerning the girls population, we found significant changes in mean values of HDL also toward higher values over 15 years of follow-up, indicating more favourable lipid profile in term of greater protection for female population at school age. Beside mean values, the results were presented in percentile distribution also for the 5^{th}, 25^{th}, 50^{th}, 75^{th} and 95^{th} percentile, separately for boys and girl. Given the results from observed parameters we have found that frequency of metabolic syndrome in school children population included in the YUSAD study was less than frequency reported in the literature.

Genetic parameters (1.2):

In the YUSAD study we have evaluated the influence of mean values of certain lipid fractions (cholesterol, HDL fraction, LDL fraction and Triglycerides) on apo-E genotype distribution. It was shown that there is increase in mean values of total cholesterol and LDL fractions from E2 genotype to E4 genotype in evaluated population. Concerning triglycerides levels we found that they differ in mean values in different apo-E genotypes. Since there are studies suggesting possible correlation between apo-E polymorphisms and subclinical markers of atherosclerosis (Intima

Media Thickness (IMT), Carotid artery compliance (CAC), further investigations in our study will include evaluation of these parameters as well.

Regarding MTHFR677 genotype, we found that there is joint correlation between MTHFG677 polymorphism and gender on diastolic blood pressure values. Both genders of evaluated population with MTHFR677TT have increased values of LDL, while only boys with TT genotype have significantly increased total cholesterol values.

Physical activity (2.7):

In the YUSAD study we have demonstrated that there is significant increase in proportion of school children that are physically active less than 3 hours a day over 15 years of follow-up, while for those that were physically active far more, we observed negative trend over the 15 years period in the proportion of these participants. Further, we have also found no significant correlation between trends of changes of blood pressure (systolic and diastolic) and lipid parameters with physical activity, inversions in correlation stress out the possible presence of other factors along with physical activity (hormones, metabolism, etc.). Given the fact above, it can be seen that school children from YUSAD study are physically active in moderate range, with preference given to those from rural places.

Future tasks and considerations

The YUSAD study is a longitudinal prospective study, with confirmed further follow-up examination for the 2012/2013 year on same population across Serbia. At the Scientific Board meeting, it was proposed to introduce further parameters in evaluation such as: ITM, inflammatory markers and other.

It is our opinion that the results obtained after the 4th evaluation will give more insights about the multi-factorial influence on atherosclerotic processes in individuals, therefore it is our task to evaluate the observed population. The particular sensitivity of obtained results is reflected by the fact that we have the trends and referential values both from school children period, adolescents and on future 4th follow-up from young adults.

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