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**Kardiovaskularne bolesti i oralno zdravlje – uticaj
oralnog zdravlja trudnica na kardiovaskularno
zdravlje djece: Cardiovascular diseases and oral
health – the impact of pregnant women’s oral health
on children’s cardiovascular health**

Mesihović Dinarević, Senka

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Poglavlje VII. PUBLIKACIJE PROJEKTA



Prevention of Cardiovascular Disease from an Early Age

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Introduction

Atherosclerosis is the most frequent disease of arteries characterized by lumen reduction of blood vessel due to local thickening of internal blood vessel by plaque/atheroma [1-3]. It is now one of the leading causes of death in developed countries. Of the ten most common causes of death, diseases of the heart and blood vessels, as a result of atherosclerosis, accounts for six of them. Atherosclerosis begins in childhood, the patient goes a long time without developing symptoms, increasing with age and at about 50 years of age, atherosclerosis seriously begins to threaten health. As a cardiovascular disease, atherosclerosis is an interdisciplinary problem that is treated by: cardiologists, neurologists, epidemiologists, nutritionists etc.

Pathophysiology

Pathophysiology of this disease concerns damaged cells that line the inner surface of the arteries the endothelium, due to chemical or mechanical damage [4]. Elevated blood cholesterol, smoking, or elevated homocysteine are examples of chemical and mechanical damage to the cells as well as high blood pressure, damage of the catheter during diagnostic procedures or even infections. Hypertension causes the formation of plaque in places where electricity hits the wall of the blood vessel and creates vortices, namely: the aortic arch, bifurcation, arteries, initial parts of the heart or coronary arteries, but also long-term or frequent spasms and immunological mechanisms lead to endothelium damage. The defect site develops inflammation and damaged endothelial cells secrete a variety of substances that attract other cells in the environment, cholesterol, platelets, smooth muscle cells, and by various interactions do accumulate in the walls of arteries. The first stage of the development of atherosclerosis occurs in the form of a "fatty streak." It is totally reversible, which means that with cessation of activities associated with harmful pathogens, endothelial cells can recover completely. However, if exposure to adverse events continues, atherosclerotic plaque grows further narrowing lumen. Consequently, reduced blood flow and tissue oxygen supply become insufficient. In the blood vessel, itself due to reduced elasticity, an increase of blood pressure occurs [5]. Elevated blood pressure can lead to: bursting in blood of the coat or its stratification with the formation of aneurysms or plaque, which can calcify and slim down the wall of the vessel with the ability of forming a clot. For atherosclerotic disease, itself plaque composition rather than its size is much more important. Plaque is primarily built of lipids, has a thin cap, hat plaque, and is easier to shoot. If thrombi are formed they can clot arteries. In contrast, larger plaque with a hard cap, which contains less fat, can rarely explode, because it is more stable.

Important risk factors

The most important risk factors for the development of atherosclerotic disease are: hyperlipidaemia, hypertension, smoking, diabetes, high fibrinogen, male sex at a younger and middle age, menopause in women taking oral contraceptives or hormone replacement therapy only with the presence of other risk factors, excessive weight, increased levels of homocysteine, physical inactivity, heredity and immune response in some diseases [6,7].

Consequences of atherosclerosis

The Consequences of atherosclerosis are: coronary or ischemic heart disease, especially myocardial infarction, cerebrovascular disease and cerebrovascular accidents (80% of all heart attacks and stroke due to atherosclerosis), the narrowing or blockage of peripheral arteries, carotid arteries, particularly the legs, which can even lead to the development of gangrene [8].

The process of hypertension starts in childhood. Etiopathogenetically it is multifactorial, a possible course and repercussions for health are longstanding and irreversible [9]. Normotension offers important data in contribution to health and increased blood pressure in childhood represents the site for preventive paediatric action. In a study which included 500 children, a correlation of birth weight and blood pressure in the paediatric population was conducted at the Paediatric clinic of Clinical University Centre of Sarajevo, during April-June 2003 [10]. The conclusion was that blood pressure measurement in children could serve for the detection of cardiovascular disease precursors' ages 8 to 9. The correlation of birth weight and systolic pressure exists, but not significantly. The main factors that influence birth weight are: sex (boys were heavier than girls up to 98 g $p < 0.05$), gestational age (preterm were lighter for 600 g $p < 0.001$), and smoking of pregnant mothers (newborns were for 219 g of lower birth weight in relation to mothers who did not smoke $p < 0.01$). Obese participants (important hypertension factor) have increased systolic blood pressure for 5.38 mmHg in relation to those participants with normal blood tension ($p < 0.01$).

Dislipoproteinaemias and repercussions on the myocardium and blood vessels in the paediatric population, represent an imperative for modern investigation. Basic investigation of lipoproteins, apolipoprotein's metabolism, the biology of the atheromatous process development in cells, and the role of genetics in the development of disease of coronary arteries is necessary in the field of preventive cardiology. Arteriosclerosis, multifactorial in its etiopathogenesis, course and repercussions, demands action from a team of physicians with the aim of early detection and treatment of dislipoproteinaemias and the reduction of the development of risk factors for coronary disease. As atherosclerosis is one of the leading causes of death in society, it represents a responsibility for all paediatricians who should do a screening of lipid levels for all children aged two with a positive family history, as well as children in schools. Dislipoproteinaemia is detectable in neonatal age, so the data from Sarajevo's study from 1991, one of the first investigations in the field of preventive cardiology in Europe, points to an elevation of total cholesterol levels, as well as an increase of apo B lipoprotein fraction [11]. In this study, the lipoprotein serum

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level was evaluated in 163 patients without positive family history of cardiovascular risk factors. The control group was comprised of 32 healthy children. In children with cardiovascular disease (congenital heart disease, rhythm disorders, rheumatic fevers), in relation to the control group, an increase of c lipid fraction (triglyceride and LDLP) with a decrease of protective fraction of HDL with statistical significance was proven, adding to increased risk for cardiovascular diseases.

Since there is no specific cure for atherosclerosis, the best way to avoid this disease is prevention. In the United States and Western Europe, where risk factors have been preventively eliminated for a long time, mortality rates "fell" below 50%. Prevention included avoiding risk factors: instead of obesity subjects should have normal body weight according to sex, age and height, work out or quick walk at least half an hour each day, because 40% of our bodies are comprised of skeletal muscles that are designed to move [6]. The primary intention of prevention is to preclude the occurrence of risk factors for atherosclerosis, and the secondary is to prevent the development or aggravation of the illness along with the reduction or control of existing risks. Primary prevention should begin as early as possible, even in childhood, creating a healthy diet, eliminating smoking, regular physical activity, which will prevent or at least slow the development of atherosclerosis. In modern medicine, there are a growing number of studies that show that children are overweight, which is certainly an adolescent risk factor for many chronic diseases including: cardiovascular, diabetes type 2, orthopaedic and psychological illnesses. The epidemic of obesity is one of the most serious health problems of today. During the past two decades, the prevalence of obesity in European countries has increased threefold. Fifty percent of adults today are overweight and a third of the European population is obese. Statistics from the Centre for Disease Control and Prevention (CDC) also speak to the tripling of the number of obese people in the last 20 years [12]. Sixteen percent of children and adolescents aged 6-19 years are overweight. Approximately 60% to 85% of obese children become obese adults, leading to an earlier and more frequent occurrence of chronic non-communicable disease. Though genetic and hormonal factors are possible causes of children being overweight and obese, excessive food intake and low physical activity are undoubtedly the main reasons for the emergence of obesity. Sitting in front of TV and computer whilst consuming calorie rich fast foods and sweetened beverages create long-term imbalances between the introduction and consumption of energy in the body. The result of this imbalance is being overweight [13,14]. Parameters for the most precise estimate of obesity is the body mass index (BMI), which is the ratio of body weight and the square of body height in kg/m². Obese people have a BMI greater than the 95th percentile. Factors related to the start of obesity are: a modified diet, reduced physical activity, and increased inactivity. The alarming trend of the expanding epidemic of obesity, particularly an increase in prevalence among young people, presents each community with a problem that has enormous economic and social consequences [15-20]. Global measures for the prevention of obesity for the countries of the European region are given in the European Charter of countering Obesity in 2006 [21].

Finding the most effective preventive measures for obesity in each country requires accurate epidemiological data on the number of obese children and adolescents, and their dietary habits and activity, which was one of the goals important research carried out in 2008-2010 in Canton Sarajevo [14]. The results of this massive study of risk factors for cardiovascular disease (the largest of it's kind in Bosnia and Herzegovina), which was carried out in Canton Sarajevo, from the earliest ages-children in kindergartens, primary and secondary school students

and the working age population, practically ages 0-65, a total of 42,828 respondents were surveyed. Through results from this research, we got the data on: risk factors for cardiovascular disease and atherosclerosis, including the level of physical activity in school environments, and the possibility of prevention, diagnosing and treating to this problem using a modern approach through cognitive behavioural aspects. For the assessment of the nutritional state of children and adolescents we used the body mass index, the degree of nutrition is obtained automatically based on CDC criteria: BMI < 5 percentile malnutrition, BMI: 5 and 85 percentile normal BW, BMI: 85-95 over nutrition, BMI greater than 95 percentile obesity. The representative sample of students in elementary and secondary schools in Canton Sarajevo were selected via random sample selection. The number of respondents in all elementary (1-8) and secondary (1-4) grades was balanced. Pupils were interviewed in written form. The survey forms were originally designed and included questions about their habits in food intake (frequency, quantity and types) and fluids, and the frequency and intensity of physical activity. The survey forms for primary and secondary schools contained similar questions but were adapted to the age group of specific subjects: lower elementary grades, higher grades of elementary school and secondary school students. Measurements of anthropometric parameters: height and weight, was done for all subjects. Height was measured using a vertical scale in centimetres (cm), and the results are rounded to 0.5 cm. Body weight was measured by electronic floor scales in kilograms (kg), and the results are rounded to 0.5 kg. The research team consisted of two physicians and two graduate nurses. The research was concluded by 2 teams. Subjects voluntarily participated in the survey and measurements the data after being input into the information system was made anonymous from all subjects. The survey and measurements of anthropometric parameters was performed in a total of 3608 students from Canton Sarajevo of which: 2329 were from 9 elementary schools and 1279 from 6 high schools. The results were: about 1/4 of children in the first 4 years are obese, and in higher classes 1/5 of pupils. According to the results of the questionnaire a majority children do not eat healthy food at home. There is a problem at school concerning eating habits: pupils from lower classes eat food from school and a majority eat food from bakeries (43.31%). Physical activity was documented in 19.92% of younger children. In the older groups of pupils there is a greater percentage of pupils who sit in front of the TV and PC for up to 2 hours (30.56%) they were also sitting during learning which means the majority of the day. A great number of pupils (58.15%) eats sweets every day between meals (Tables 1-6).

Conclusion

In Conclusion, the question raised is: what to do about the prevention of cardiovascular disease? Why do schools need to worry about health? As a society, we value good health. Good health is necessary for effective learning. Healthy students become healthy, productive citizens. Schools are the places where we spend most of our youth so we have to initiate a change. The teamwork of an environmental society and new policies are needed. As a priority, we should create a place for physical activity and nutrition in schools; develop funded prevention programs and a systematic approach to the problem. Point to the problem of obesity in an adequate manner, and create partnerships with value to the social community in creating a healthy lifestyle. Schools can provide: quality physical education classes, healthy nutrition campaigns, parenting education, psychosocial education/intervention with nutrition strategy. Prevention is the key! It is necessary to establish dialogue in cardiovascular medicine. Prevention of obesity consists of nutrition conducted according to modern guidelines in relation to the input of: carbohydrates, fats, proteins, vitamins and fluids. It is necessary to

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School class	Total number of students	M	F	BMI classification			
				Under Weight (%)	Normal weight (%)	Over weight (%)	Obesity (%)
I-IV Elementary School	1077	546	531	T: 20,86 M: 7,72 F: 13,14	T: 55,26 M: 28,68 F: 26,58	T: 12,28 M: 7,47 F: 4,81	T: 11,58 M: 6,77 F: 4,81
V-VIII Elementary School	1252	680	572	T: 9,16 M: 4,65 F: 4,51	T: 69,80 M: 37,98 F: 31,82	T: 13,07 M: 7,49 F: 5,58	T: 8,00 M: 3,69 F: 4,31
I-IV High School	1279	531	748	T: 6,76 M: 1,31 F: 5,45	T: 80,43 M: 34,15 F: 46,28	T: 9,55 M: 5,18 F: 4,37	T: 3,24 M: 1,47 F: 1,77
All schools	3608	1757	1851	T: 12,49 M: 4,63 F: 7,86	T: 68,74 M: 33,60 F: 35,14	T: 11,86 M: 6,71 F: 5,15	T: 6,86 M: 1,32 F: 5,54

Table 1: BMI classification of students according to grades, schools and gender.

School and class	Homemade sandwich (%)	Sandwich bought at school (%)	Food from the bakery (%)	Snacks (%)	I don't eat at school (%)
I-IV Elementary School	30,69	44,63	5,04	17,68	1,98
V-VIII Elementary School	16,57	24,62	42,67	10,96	5,27
I-IV High School	2,70	41,09	42,01	8,89	5,37
All schools	16,65	36,78	29,90	12,57	4,20

Table 2: Distribution of the quality nutrition of students in school.

School class	Water (%)	Juices (%)	Milk (%)	Sodas (%)
I-IV Elementary School	50,88	23,19	23,37	2,6
V-VIII Elementary School	54,94	21,71	12,45	11,87
I-IV High School	49,35	16,77	13,19	20,72
All schools	51,82	20,65	16,43	11,05

Table 3: Distribution of types of beverages that students drink during the day.

School class	Candys every day (%)	Sometimes and rarely (%)
I-IV Elementary School	30,89	59,11
V-VIII Elementary School	64,53	33,47
I-IV High School	80,85	19,15
All schools	58,15	31,24

Table 4: Distribution of prevalence of candy consuming.

School class	Every day activity (%)	Activity only on sport class (%)	Activity 2-3x per week (%)	Rarely (%)
I-IV Elementary School	19,92	39,05	40,36	0,00
V-VIII Elementary School	36,42	27,56	24,52	11,50
I-IV High School	46,89	29,19	18,08	5,65
All schools	31,07	31,93	27,65	8,51

Table 5: Distribution of the degree of sports activities.

School class	< 1 hour (%)	1-2 hours (%)	2-3 hours (%)	3 hours (%)
I-IV Elementary School	23,60	36,62	18,51	20,89
V-VIII Elementary School	13,81	30,56	27,74	27,96
I-IV High School	18,70	33,59	23,12	24,42

Table 6: Distribution of the length of time spent in front of computer and TV.

maintain regular physical activity, both in school and in free time. It is also necessary to promote of continuous education about healthy eating and a healthy lifestyle (activity, not smoking) in all primary and secondary schools in the country, the engagement of teams of family doctors to monitor the nutritional status of school children and youth.

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The challenges of detecting risk factors for the development of atherosclerosis

Senka Mesihović-Dinarević, Lutvo Sporišević, Berislav Topić, Sanja Jurišić, Senad Saric, Britt Gritt, Vjekoslav Krželj, Anes Jogunčić, Samir Prohić and Aida Ramić

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The most frequent disease of the arteries is atherosclerosis which is characterized by lumen reduction of blood vessels due to local thickening of internal blood vessels caused by plaque / atheroma [1-3]. Atherosclerosis is now one of the leading causes of death in developed countries. The most important risk factors for the development of atherosclerotic disease are: hyperlipidaemia, hypertension, smoking, diabetes, high fibrinogen, excessive weight and physical inactivity [4,5]. Some authors pointed out the possible connection between periodontal disease in pregnant women with risk of preterm delivery, newborns of low gestational age with low birth masses and possible cardiovascular diseases [6-10]. Bearing this in mind, there is ongoing study in the Balkan region with the aim of investigating more predictors of early cardiovascular risk / increased body mass index, high values of blood pressure and thickening of intima-media carotids complex/ in comparison to children whose mothers had good oral health during pregnancy. Preliminary study data: mean age of 43 pregnant women is 30.7+/-5.7 years, 90.3% pregnancy runs properly, KEP index: 12.32+/-5.7, plak index 0.312, restored teeth 65.62%; eating habits: 48.4% dairy products, fruit 64.5%, vegetables 22.6%, meat 41.9%, fish in 35.2%. Regular dental therapy can decrease frequency of caries, periodontal disease in pregnant women, the frequency of prematurity, low birth weight (with all its potential complications, decreasing financial costs of neonatal intensive care management and cardiovascular repercussions on newborn's health). A cardiovascular-oral health data base for the Balkan region can be used as a geographic, demographic and epidemiologic source of information for the detection and identification of new potential risk factors of individuals for preterm delivery and possible atherosclerosis. Primary prevention of atherosclerosis should begin as early as possible, during pregnancy, in childhood, creating a healthy way of life, which will be able to prevent or at least slow the development of atherosclerosis.

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Biography

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ORAL AND CARDIOVASCULAR HEALTH- THE CHALLENGES OF DETECTING RISK FACTORS FOR THE DEVELOPMENT OF ATHEROSCLEROSIS

Senka Mesihović-Dinarević*, Lutvo Sporišević, Berislav Topić, Sanja Jurišić, Senad Saric, Grit Kirsten-Sarić, Vjekoslav Krželj, Anes Jogunčić, Samir Prohić, Aida Ramić

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The Challenges of Detecting Risk Factors for the Development of Atherosclerosis

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Abstract

The most frequent disease of the arteries is atherosclerosis which is characterized by lumen reduction of blood vessels due to local thickening of internal blood vessels caused by plaque/atheroma. As a cardiovascular disease, atherosclerosis is an interdisciplinary problem and one of the leading causes of death in developed countries. It begins in childhood, goes a long time without manifesting symptoms, increasing with age it begins to seriously threaten health. The most dangerous risk factors for the development of atherosclerotic disease are: Hyperlipidaemia, hypertension, smoking, diabetes, high fibrinogen, excessive weight and physical inactivity.

Keywords: Atherosclerosis; Hyperlipidaemia; Hypertension; Myocardial infarction; Parodontal disease

Introduction

The primary intention of prevention of atherosclerosis is to preclude the occurrence of risk factors for atherosclerosis, and the secondary is to prevent the development or aggravation of the illness along with the reduction or control of existing risks. Primary prevention should begin as early as possible, even in childhood, creating a healthy diet, eliminating smoking, regular physical activity, which will prevent or at least slow the development of atherosclerosis. The consequences of atherosclerosis are: coronary or ischemic heart disease, especially myocardial infarction, cerebrovascular disease and cerebrovascular accident (80% of all heart attacks and brain due to atherosclerosis), narrowing or blockage of peripheral arteries, carotid arteries. Since there is no specific cure for atherosclerosis, the best way to prevent this disease, is prevention.

Some authors pointed out the possible connection between parodontal disease in pregnant women with the risk of preterm delivery, new-borns of low gestational age with low birth masses and possible cardiovascular disease [1-7].

Oral health

Appropriate oral health reflects and influences general health and the quality of life. The oral cavity is an integral part of the human organism and therefore there exists a great connection between oral health and systemic health. Not only do some systemic diseases such as diabetes, osteoporosis, HIV infection, trisomy 21 have a predisposition for periodontitis but an opposite applies. Susceptibility to certain systemic disease is higher in patients with periodontitis than in healthy people: chronic periodontitis is a risk factor for future cardiovascular disease, pregnant women with chronic periodontitis have more frequent have preterm birth and new-borns have a low birth weight. The explanation for the pathophysiological mechanisms of parodont focus and systemic disease is associated with elevated levels of circulating pro-inflammatory cytokines and prostaglandins derived from: diseased parodont, gram negative bacteria and their endotoxin-like substances, that appear from subgingival biofilms immediately entering the bloodstream. The dominant problems of everyday dental practice are: caries, periodontal disease, occlusal abnormalities, the relationship of oral and general health and a holistic approach to the patient. Caries and periodontal disease are of an infectious aetiology therefore the prevention of dental caries and periodontal disease means preventing odontogenic focuses. A periodontal pocket is a risk factor for the development or worsening of systemic - focal

disease, because the infection is always present in it; a pocket flora is various, massive, virulent and penetrates the soft wall of the pocket, the pocket is under constant mechanical stimulation during chewing, swallowing and speech, all of which favour the penetration of bacteria into circulation and the formation of transient bacteremia. Dental caries and periodontal disease are the most common and significant oral disease, they can cause and aggravate numerous other disease: of the cardiovascular system (infective endocarditis, atherosclerosis, myocarditis and myocardial infarction), of the respiratory system (pneumonia, chronic obstructive pulmonary disease, bronchial asthma and pulmonary abscess), neurological disorders (cerebral infarction and cerebral abscess), diabetes mellitus, rheumatoid arthritis, Alzheimer's disease, and other illnesses) [8]. Interdisciplinary cooperation in the elimination of potential negative effects of periodontal infections will result in better systemic health. Atherosclerosis is the basis for all cardiovascular disease. Periodontal pathogens can directly infect the vascular endothelium and atherosclerotic plaque causing inflammation. Then, they are capable of producing a variety of virulence factors (adhesions, haemolysis), which have adverse effects on the vascular system resulting in platelet aggregation and adhesion; in addition, lipid clusters are formed with deposits of cholesterol that contribute to atheroma formation. The treatment of chronic periodontitis reduces systemic inflammation factors.

Pregnancy

Pregnancy is a state in which there are complex physical and physiological changes, which have important effects on multiple systems of organs. High levels of circulating oestrogen during pregnancy are associated with high incidence of gingivitis and gingival hyperplasia or certain forms of periodontal disease [9]. It is believed that approximately 40% of pregnant women have a certain form of periodontal disease [8-10]. Offenbacher et al. first suggested a possible link between periodontal disease and risks for child delivery of a low

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gestational age or small birth weight [11]. Many researchers suggest a possible link between periodontal disease in pregnant women with a risk for preterm delivery, respectively, the birth of babies with low birth weight. Researches show that in pregnant women with periodontal disease there is a 2-7 times higher risk for prematurity. Morre et al. found a large number of foetal deaths among mothers with periodontal disease [12]. However, a focal infection may affect prematurity (birth before 37 weeks gestation) of neonates and neonatal reduction in weight (weight <2500 gm). Bacteraemia of periodontal pathogens transplacental can lead to intrauterine infection. Proinflammatory cytokines release the (LPS) endotoxin that precipitates in premature labour. LPS - bacterial lipopolysaccharides, are the major molecular component of the outer membrane of Gram-negative bacteria and serve as a physical barrier providing the bacteria protection from its surroundings. That is why dentists need to motivate, educate and instruct pregnant women towards a higher level of oral hygiene and to repair all dento-oral lesions in dental therapeutic procedures, especially periodontal pockets, thereby reducing the number of premature births. It is believed that the Gram-negative anaerobic bacteria, present in the periodontal tissue, can be a source for endotoxin and lipopolysaccharides, that lead to high levels of inflammatory mediators - interleukin-6 (IL-6), interleukin-8 (IL-8), Interleukin-1 beta (IL-1β), and prostaglandin E2 (PGE2) and tumor necrosis factor-α (TNF-α), which are transferred to the uterus, cervix and placenta causing premature birth or the birth of children of a small birth weight. Jeffcoat et al. whilst investigating the connection between periodontal disease of pregnant women and preterm birth in group of 1313 pregnant women, found that a moderate to severe form of periodontal disease, diagnosed in early pregnancy, was associated with an increased risk for premature delivery, independently of other traditional risk factors for prematurity [13]. During pregnancy, there is an increased susceptibility to caries due to: the increased acidity of the oral cavity, the increased consumption of refined sugars and poor oral hygiene [14]. Caries bacteria in children are usually transmitted by direct transmission through the mother's saliva. Mothers with high titres of *Streptococcus* mutants in their saliva are going to substantially transmit the bacteria to their baby - by vertical transmission, creating conditions for early childhood caries. Of course, the time and frequency of the transmission of bacteria, the child's preference for the accumulation of bacteria on its teeth, the composition and flow of the child's saliva, the amount of refined sugar in the baby's food, are all significant predictors of early children's caries [15]. The incidence of births of premature infants and new-borns of a small birth weight is between 5-18%, depending on the geographical area and population characteristics. Due to the immaturity of their organ systems, premature babies and infants of a small birth weight are among in vulnerable group of infants - complications due to prematurity are the leading cause of death in children under five years of age [16]. It is very important to determine risk factors that can lead to the risk of the prematurity of new-borns and new-borns of a small birth weight, i.e. with knowledge of the risk factors, it is possible to substantially eliminate or reduce the risk of premature baby birth or the birth of children with a small weight and to decrease the rate of perinatal mortality and possible complications. Preterm children or infants of a small birth weight exhibit a higher incidence of cardiovascular risk factors (obesity, hypertension, dyslipidaemia), and type 2 diabetes mellitus [16]. Animal and epidemiological studies indicate that conditions of elevated levels of glucocorticoids intrauterine during life, programme the hypothalamus-pituitary-adrenal gland axis that plays a key role in the higher incidence of cardiovascular risk in premature infants and children of a small birth weight [17]. Apart from the role of microbiome mouth (microbiome

- all microbes, their genome and mutual interaction in a particular environment) as a risk factor for premature delivery or the birth of new-born of small birth weight, it is possible that the microorganisms of the oral cavity condition chronic inflammation that can represent an atherosclerotic cardiovascular risk factor. Adequate prenatal care should include oral health care of pregnant women, i.e. for pregnant women, there is a need to point out the importance of practicing regular oral hygiene and the need for periodic or as many as or as frequently as needed dental check-ups. The sufficient screening/screening of oral health status of pregnant women is not carried out in daily work, so with screening status of oral health in a greater number of pregnant women, including the assessment of oral hygiene, we would be able to timely identify pregnant women who have dental caries respectively periodontal disease [18]. With timely dental treatment we could reduce the incidence of dental caries and periodontal disease in pregnant women and may reduce the incidence of preterm delivery and the birth of new-borns of a small birth weight, an early childhood caries and predictors of early atherosclerotic cardiovascular risk (increased body mass index, blood pressure and thickening of the carotid intima-media complex). In a cohort of children, who are preterm or have a low birth weight, a certain number of children age 3 have a greater body mass index, a higher value of systolic and diastolic blood pressure, as well as a thickening of the intima-media complex of the carotid artery with incipient signs of cardiovascular system disease [19].

Insufficient insight into the possible pathological implications of the oral health status of pregnant women to premature expression of cardiovascular risk factors in children, initiated this research.

The impact of oral health of pregnant women on the cardiovascular health of children is a Project within the South-eastern European region that runs by the Committee of the Cardiovascular Disease Department of Medical Sciences of Academy of Arts and Sciences of Bosnia and Herzegovina. During 2017, the first phase of research was completed according to plan/lasted for 12 months. In this study 43 pregnant women from Bosnia and Herzegovina and Croatia were included.

The Project's Common Goals are to Give Answers to

Does and in what capacity the oral health of pregnant women influence pregnancy? Does insufficient oral health of pregnant women (periodontal disease and certain forms of caries) influence gestational age, birth mass of children or oral and cardiovascular health of new-born's, infants and small children? Is chronic inflammation of the oral cavity (periodontal disease and caries) in pregnant women a atherosclerotic and cardiovascular risk factor, that is; do preschool children whose mothers during pregnancy had periodontal disease and/or caries, have a more prominent predictor of early cardiovascular risk (increased body mass index, high value of blood pressure and thickening of intima-media carotids complex) in comparison to children whose mothers during pregnancy had good oral health?

To achieve these goals, we are conducting the research that can last up to 48 months, using a multidisciplinary approach which includes: A gynaecologist, a dentist, a paediatrician, a radiologist, a cardiologist, nutritionists, epidemiologists and statistics. These examinations integrated research from 3 respected centres in Bosnia and Herzegovina and Croatia using combined experience and skills. The aim of this research is to investigate more prominent predictors of early cardiovascular risk increased body mass index, high values of blood pressure and the thickening of the intima-media carotids complex in comparison to children whose mothers had good oral health during pregnancy.

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We are presenting the data on the I phase of this Project conducted in: Sarajevo, Mostar, and Split. The plan is to finish project in 2019 the II phase, and in 2020 the III phase.

The Survey is Designed as a Cohort Study

It included mothers/pregnant women selected by random selection (randomized sampling). During regular gynaecological and obstetric examination (being I trimester, if necessary, II and III trimester of gestation) a suggestion was given to pregnant women to do their dental examination in order to assess their oral health status. The general health status of the pregnant women was determined on the basis of an assessment of their medical records. The research did not include: Pregnant women with cardiovascular diseases, diabetes mellitus, kidney disease or any chronic illnesses. The survey testing assesses the habits of pregnant women: eating habits, physical activity, alcohol consumption, drugs and smoking.

II phase: The children would be evaluated as new-borns, preterm infants, new-borns of a desirable body weight and new-born of a small birth weight, they would be followed up to their third or fourth year of life. During the systematic review (the first month of life, the first year, the third and fourth year of life) paediatricians should evaluate: the basic characteristics related to pregnancy and childbirth, analysis of the eating habits of children, anthropometric parameters, determine blood pressure values and while radiologists determine the value of complex

intima-media carotid artery a cardiologist by echocardiography would evaluate the hemodynamic status of the respondents. The study would include children of proper health conditions, i.e. children with congenital anomalies or certain chronic illnesses would be excluded from the study. Dentists would judge the status of dental health of pregnant women and children and evaluate the appropriateness of the oral health of pregnant women and children. The research is based on the principles of the Helsinki Declaration from 1975 and its amendments in 2008. In order to implement the principles of ethical and bioethical research consent/approval of the appropriate ethics committees/commissions is required. Voluntary inclusion of pregnant women and children is confirmed by signing an informed consent form.

Materials and Methods

After signing the informed consent form i.e. informing mothers/pregnant women, by research methodology the following tests are conducted I phase: - survey testing - dental examination. Evaluation of general health conditions and life habits of pregnant women, determining the basic core characteristics of oral health protection during pregnancy.

N	43
Age (mean)	30.7 ± 5.7
Pregnancy status	
Normal	39 (90.70%)
With complications	4 (9.30%)
Education status	
High school	8 (18.60%)
Senior high school	4 (9.30%)
University education	31 (72.10%)
Diseases during pregnancy	
Without	37 (86.05%)
Rare/Lighter illnesses	4 (9.3%)
With bigger complications	2 (4.65%)
How often do you brush your teeth?	
At least 2 × per day	27 (62.8%)
After each meal	16 (37.2%)
How long it takes to brush your teeth?	
Between 1 and 3 min	28 (65.12%)
Longer than 3 min	14 (32.56%)
At most one minute	1 (2.32%)
When do you brush your teeth?	
After each meal	7 (16.3%)
In the morning	1 (2.3%)
In the evening	3 (6.98%)
In the morning and in the evening	32 (74.42%)
The most common reason for dental visit	
Tooth repair	35%
Regular control	53%
Dental pain	12%
How many times did you visit a dentist last year?	
1 ×	23%
2 ×	46%
Not remembering	12%
Didn't visit a dentist	19%

Table 1: Dental status.

Fruit	
>2 per day	65%
1 × per day	30%
Several times per week	5%
Milk and milk products	
>2 per day	33%
1 × per day	49%
1 × per week	0%
Several times per week	9%
Rarely or never	9%
Vegetables	
1 × per day	58%
>2 per day	23%
1 × per week	5%
Several times per week	14%
Juices	
2+ per day	25%
1 × per day	26%
1 × per week	14%
Several times per week	7%
Rarely or never	28%
Sweets	
1 × per day	28%
1 × per week	5%
2+ per day	23%
Several times per week	28%
Rarely or never	16%
Meat	
2+ per day	25%
1 × per day	26%
1 × per week	14%
Several times per week	14%
Rarely or never	21%
Fish	
2+ per day	5%
1 × per day	9%
1 × per week	46%
Several times per week	14%
Rarely or never	26%

Table 2: Eating habits.

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KEP index	12.32 ± 5.729		Plaque index		0.3125 ± 0.405	
	S1	S2	S3	S4	S5	S6
A healthy periodontal	42.90%	82.10%	39.30%	53.60%	71.40%	35.70%
Bleeding	42.90%	14.30%	46.40%	35.40%	25%	53.60%
Calculus	7.10%	3.60%	7.15%	7.20%	3.60%	10.70%
Periodontal pocket (4-5 mm)	7.10%		7.15%	3.80%	--	--

Table 3: KEP index.

IDB		[] [] [] []	
Date		[] [] [] / [] [] [] / 2017.	
Institution:			
City:			
State:			
Telephone:		Mail:	
1. GENERAL DATA			
1.1. Birth year			
1.2. Your educational status	Primary school ☐	High school ☐	Higher school ☐ Faculty ☐ ☐ Other:
1.3. Your work status	Employed ☐	Unemployed ☐	
1.4. According to your estimation, your family's economical status is:	Below the average ☐	Average ☐	Above average ☐
1.5. In addition to this child, you:	You have no other children ☐	I have a younger child / children (specify how much) ☐ ____ I have an older child / children (how many) ☐	
2. PREGNANCY DATA			
2.1. How does pregnancy go?	Orderly ☐	With complications ☐ (name them: _____)	
2.2. Diagnosed illnesses during pregnancy?	Without ☐	Early ☐	Often ☐
2.3. Do you drink alcohol during pregnancy?	Yes ☐	Sometimes ☐	No ☐
2.4. Do you smoke during pregnancy?	Yes ☐	Sometimes ☐	No ☐
Do you use drugs (medicine) during pregnancy?	Yes ☐	No ☐	
*Please name them: _____			
3. EVALUATION OF KNOWLEDGE ON ORAL HEALTH (Mark one answer to the questions below!)			
3.1. In your opinion, how often you need to brush your teeth?	At least once per day ☐	At least 2x per day ☐	After every meal ☐ It isn't necessary to brush teeth every day ☐ I don't know ☐
3.2. How long it takes to brush your teeth?	At most 1 min ☐	1-3 minutes ☐	Longer than 3 min ☐ I don't know ☐
3.3. Is it for thorough cleaning of the teeth necessary to use dental floss?	Yes ☐	No ☐	I don't know ☐
3.4. Is it necessary that the toothpaste contains fluoride contains fluoride?	Yes ☐	No ☐	I don't know ☐
EVALUATION OF ATTITUDES ABOUT ORAL HEALTH (Mark one of the questions below!)			
4.1. Condition of the tooth and the oral cavity have a negative impact on your overall health?	I agree ☐	I disagree ☐	I'm not sure ☐
4.2. Regular inspection of the teeth and oral cavity is important for the prevention of dental caries and periodontal disease?	I agree ☐	I disagree ☐	I'm not sure ☐
4.3. Inappropriate state of your dental health can lead to premature birth or having a baby low birth weight?	I agree ☐	I disagree ☐	I'm not sure ☐
4.4. Inappropriate state of your dental health can lead to problems with dental health of your child or some other disease?	I agree ☐	I disagree ☐	I'm not sure ☐
4.5. Regular dental examinations are necessary during pregnancy?	I agree ☐	I disagree ☐	I'm not sure ☐
4.6. Dental interventions are safe during pregnancy?	I agree ☐	I disagree ☐	I'm not sure ☐
5. EVALUATION OF PRACTICE ON ORAL HEALTH (Mark one of the questions below!)			
5.1. How often do you brush your teeth?	Only in the morning ☐	Only before sleep at night ☐	In the morning and in the night ☐ After every meal ☐ I don't brush teeth every day ☐

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5.2. How long do you brush your teeth?	1 minute ☐	1-3 minutes ☐	>3 minutes ☐		
5.3. Do you use dental floss?	Da ☐			Ne ☐	
5.4. Do you use antibacterial mouthwashes?	Da ☐			Ne ☐	
5.5. Do you use chewing gum?	Da ☐			Ne ☐	
5.6. If you use chewing gum, specify which chewing gum you are using?	Chewing gum with xylitol ☐	Chewing gum with sugar ☐	Chewing gum without sugar ☐	I use any kind of chewing gum ☐	
5.7. How many times did you have a regular visit to the dentist last year?	1x ☐	2x ☐	I did not visit dentist ☐		I can not remember ☐
5.8. The most common reason to visit a dentist is?	regular inspection of the dental health ☐	because of dental pain ☐	tooth extraction ☐	tooth repair ☐	due to other reasons ☐ Please, specify:
5.9. How many daily meals do you have?	1-2 ☐	3 meals ☐	4 meals ☐	5 meals ☐	>5 meals ☐
5.10. How often do you consume the following foods?					
Grocery	≥ 2 daily	1x day	Several times per week/weekly	1x per week	Rarely or never
Milk or dairy products					
Fruit					
Vegetables					
Fruit juices					
Non-alcoholic drinks					
Sweets (sugar, sweet)					
(Cakes, Biscuits and Chocolate)					
Honey, jam and various spreads					
Candies					
Chips, sticks and other snacks					
Meat					
Fish					
Eggs					
5.11. The most common source of information on tooth health and oral cavity I find out?					
	From dentist ☐	From medias ☐	Internet (web pages) ☐	Friends and society ☐	
Signature: _____ Thank you very much for your time!					

Figure 1: Questionnaire for mother: The impact of oral health of pregnant women on the cardiovascular health of children.

Techniques of research

Originally created questionnaires for mothers/pregnant women and children (general data, data from personal history, data on eating habits, data on harmful habits, data on physical activities and data on oral health); determination of initial caries, periodontal examination with complete examination of the oral cavity in mothers and children according to WHO recommendations; determination of body mass and height, calculation of body mass index; determination of blood pressure values in children; determination of carotid complex of intima-media artery by 2D Colour Doppler ultrasonography; 2D Colour Doppler echocardiography evaluation of the cardiovascular system; data base creation in MS Access or MS Office; evaluation of variables by statistical programs in consultation with statisticians; design and development of a web based data collection system for research data entry and analysis.

Survey sheets were originally designed, they include questions about their habits in food intake (frequency, quantity and types) and fluids with a Questioner of dental status in mothers (Figures 1-3).

Anonymous questionnaire for gynecologists and dentists

As a dentist, I avoid the application of local anaesthesia with adrenalin to pregnant women during all months of pregnancy? I avoid any kind of X-raying pregnant women? In pregnancy the extraction of a tooth under pain is not recommended? I avoid therapy of gravidity gingivitis in pregnant women in all phases of pregnancy? Trepanation of teeth, the cause of acute dentogen infection, and incisions are not recommended in pregnant women? The Study Workflow: Pregnant women-gynaecologist-dentist- radiologist- cardiologist-epidemiologist.

Research Data

Preliminary study data I phase (2017-18): Mean age of 43 pregnant women is 30.7 ± 5.7 years; 90.7% pregnancy ran properly; complication detected in 9.3%.

During pregnancy: 86.05% mothers had no new disease diagnosed.

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ID NUMBER			
HEALTH CARD NUMBER			
DATE OF EXAM			
A. GENERAL RISK PARAMETERS			
1. COURSE OF PREGNANCY		0 - Normal ☐	1 - Maintained ☐
2. WEIGHT DURING PREGNANCY		0 - Normal ☐	1 - gained weight over 13 kg ☐ 2 - Lost weight ☐
3. VOMITING, AS AN ACCOMPANYING SYMPTOM OF PREGNANCY:		0 - Rarely/Never ☐	1 - Daily/Often ☐
4. Dietary regimen during pregnancy:			
4a) milk and dairy products:		0 - Everyday - often ☐	1 - Rarely ☐
4b) meat-fish-eggs:		0 - Everyday - often ☐	1 - Rarely ☐
4c) fruit - vegetables:		0 - Everyday - often ☐	1 - Rarely ☐
4d) sweets (sugar, honey, sweet, candy, chocolate, cakes, etc.)		0 - Rarely/Never ☐	1 - Often ☐ 2 - Daily ☐
5. MEDICINE TAKEN IN PREGNANCY		0 - Without ☐	1 - Rarely ☐ 2 - Frequent ☐
6. DIAGNOSED DISEASE DURING PREGNANCY:		0 - Without ☐	1 - Rarely/Smaller ☐ 2 - Frequent ☐
7. FLUOR USED IN THE FORM		0 - Drinking water ☐ 1 - Pills from 4. month of pregnancy ☐	2 - Occasionally Pills ☐ 3 - Not used ☐
8. DELIVERY:		0 - As scheduled ☐	1 - Early ☐ 2 - Prematurity ☐
9. CHILDS WEIGHT AT BIRTH:		0 - Above 2.5 kg ☐	1 - Less than 2.5 kg ☐
10. MOTHER'S ORAL HEALTH		0 - Without Illness ☐ 1 - Repaired ☐	2 - Non repaired ☐
11. FATHER'S ORAL HEALTH:		0 - Without Illness ☐ 1 - Repaired ☐	2 - Non repaired ☐
Risk zone		Low Risk	0-8 points
		Middle Risk	9-16 points
		High Risk	17-23 points
B. SPECIFIC RISK PARAMETERS:			
Before health-education interventions			
After the health-education intervention			
0 - No plaque 1 - On the edge of the gingival (probe, staining) 2 - In the gingival sulcus or pocket (visible) 3 - Large quantity		Risk Zone: Pi < from Low risk Pi from to Middle risk Pi > from High risk	
B4 - Tooth Status (TS)			
Before health-education interventions			
After the health-education intervention			

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H - healthy tooth is present C - Caries R - Tooth root P - Plum CT - Cured tooth E - Tooth removed	Risk zone TS < from Low risk TS from to Middle risk TS > from High risk
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Figure 2: Questionnaires' of dental status in mothers.

IDB			
DATE	/ / 201		
INSTITUTION:			
City:			
State:			
Telephone:	Mail:		
1. GENERAL DATA			
1.1. Child's birth date			
1.2. Sex:	Male ☐	Female ☐	
2. INFORMATION ABOUT PREGNANCY AND BIRTH (Mark one of the questions below!)			
2.1. Duration of pregnancy in weeks / weeks?			
2.2. Child was born	At time ☐	Earlier ☐	Prematurity ☐
2.3. Were there any complications during pregnancy?	No ☐	Yes ☐	Name complications:
2.4. How is delivery done?	Natural ☐	Cesarean section ☐	Forces ☐ Vacuum extraction ☐
2.5. Was there any complications during delivery?	No ☐	Yes ☐	Name complications:
2.6. APGAR score	1 minute	5 minute	
2.7. Birth weight (BW) of the child	Birth length (BL) of the child		
3. ABOUT INFANT PERIOD (Mark one of the questions below!)			
3.1 Did your child in first year of life had any			
-congenital heart disease?	No ☐	Yes ☐	
-other chronic illnesses?	No ☐	Yes ☐	
* If your answer to the previous question was "Yes" to indicate which illnesses:			
3.2. Did your child have any natural feeding / breastfeeding during the first year of life?	Not breastfeeding or is breastfeeding a few months ☐		
	Exclusive breastfeeding for six months while continuing breastfeeding and the addition of non-milk foods after 6 months of age (fruits, vegetables, meat ...) ☐		
	The combination of breast feeding infant formula containing non-milk foods after 4 months of age ☐		
	Milk formula containing non-milk foods after 4 months ☐		
EVALUATION OF ORAL HEALTH KNOWLEDGE (Give one of the questions below!)			
4.1. If the mother has cavities or inappropriate oral health - states can affect the appearance of cavities in children?	Yes ☐	No ☐	I don't know ☐
4.2. Is it necessary to treat tooth decay in young children?	Yes ☐	No ☐	I don't know ☐
4.3. When children should had the first visit to the dentist?	Between 6 and 12 months of the child's life ☐		
	In the 1st child's year ☐		
	In the 2nd childhood year ☐		
	In the 3rd child's year ☐		
	When a child needs to go to the first grade ☐		
I do not know / I'm not sure ☐			
5. EVALUATION OF ATTITUDE ABOUT ORAL HEALTH (Mark one of the questions below!)			
5.1. Children with early childhood caries later may have a high probability for the decay of permanent teeth?	Yes ☐	No ☐	I'm not sure ☐
5.2. Do you frequent and prolonged night meals with milk formula can lead to the child's caries?	Yes ☐	No ☐	I'm not sure ☐
5.3. Does frequent or prolonged administration of sweetened beverages (tea, juice) can lead to baby's caries?	Yes ☐	No ☐	I'm not sure ☐

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5.4. Does the mother's kisses, or tasting food over same spoon can cause children's caries?		Yes ☐	No ☐	I'm not sure ☐
6. EVALUATION OF PRACTICE ON ORAL HEALTH (Mark one of the questions below!)				
6.1. Have you cleaned gingivas or mouth with piece of gauze swelled in water or paper after the last children's meal?		Daily ☐ Rarely ☐ Never ☐		
6.2. When did you begin brushing your child's teeth with fluoride paste?		Immediately after the eruption of teeth ☐ (month of life): At the age of (specify in months) ☐ Milk teeth - should not be brushed ☐ I do not know ☐		
6.3. How many times a day do you brush your child's teeth with flourid paste?		Only in the morning ☐ Only in the evening ☐ In the morning and in the vening ☐ Weekly ☐ Don't brush teeth ☐		
6.4. At what age (months of life) did the child have the first visit to the dentist?		None ☐ Never ☐		
6.5. In the previous year, how many times child had dental visits?		1x ☐ 2x ☐ None ☐ Multiple ☐		
6.6. The most common reason to visit a dentist is?		Regular control ☐ Dental pain ☐ Tooth removal ☐ Tooth repair ☐ Other reasons ☐ Name it: _____		
6.7. How many daily meals do you have?		1-2 ☐ 3 ☐ 4 broka ☐ 5 ☐ >5 ☐		
6.8. Specify which liquid usually takes a child?		Milk ☐ Water ☐ Tee ☐ Natural juice ☐		
6.9. How often child consumes following foods?				
Food	≥ 2 daily	1x daily	Several times a week / weakly	1x per week
Milk or dairy products				
Fruit				
Vegetables				
Fruit juice				
Non-alcoholic drinks				
Sweets (sugar, sweet)				
Cakes, Biscuits, Chocolate				
Hney, jam				
Candies				
Chips, sticks and other snacks				
Meat				
Fish				
Eggs				
6.10. The most common source of information on tooth health and oral cavity I find out?				
	From a dentist ☐	The media ☐	Internet (web) ☐	Friends, acquaintance ☐
Do you competent pediatrician recommended to take your child to the dentist?		Da ☐ Ne ☐		
Signature: _____		Thank you very much!		

Figure 3: Childs questionnaire: The impact of oral health of pregnant women on the cardiovascular health of children.

Only 9.3% of women in pregnancy had rare/lighter illnesses and 4.65% of respondents had bigger complications. Educational status: High school finished 8 (18.60%) mothers, senior high school: 4 (9.30%), university education: 31 (72.10%) pregnant women.

Eating habits: 49% dairy products: daily; fruit 65%: two or more times per day; vegetables 23%: Two or more times per day; meat 51%: daily; with 14% more that eats meat several times per week; fish in 46%: once a week; in 26% rarely or never.

KEP (Cavities/Tooth extraction/seal) index: 12.32 ± 5.7 ; plaque index 0.312; repaired teeth 65.62%; non-repaired teeth 12.5% (Tables 1-3).

Expected results and their significance

The results of this research will show that a certain number of

mothers have an inappropriate oral health status due firstly to insufficient oral hygiene, not adhering to appropriate eating guidelines and insufficient visits to the dentist. Using this research, we are going to show that a certain number of mothers with a bad oral health status deliver preterm new-born's and new-born's with low birth weight. We expect that children whose mothers had a bad oral health status age 3 have a worse oral health status in comparison to children whose mothers had a good oral health status. The group of children who are preterm or born with a low birth weight, age 3/4/years, would have a greater body mass index for their age and sex, greater values of blood pressure and greater thickening of the intima-media complex in comparison to the desired values of these parameters for term new-born's and new-borns of a desirable birth weight, with possible incipient signs of cardiovascular system disease including atherosclerotic, in comparison to the control group.

Citation: Dinarević SM, Topić B, Jurišić S, Prohić S, Sporišević L, et al. (2018) The Challenges of Detecting Risk Factors for the Development of Atherosclerosis. *J Cardiovasc Dis Diagn* 6: 342. doi: [10.4172/2329-9517.1000342](https://doi.org/10.4172/2329-9517.1000342)

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Result

Regular dental therapy can decrease the frequency of the appearance of caries, periodontal disease in pregnant women, the frequency of prematurity, low birth weight with all its potential complications, decrease the financial costs of neonatal intensive care management and cardiovascular repercussions on a new-born's health.

Discussion and Conclusion

The results so far indicate to the awareness of pregnant women of the importance of oral health and its influence on child development. However, it is necessary to wait until the end of the study to see definitive results, the impact of mother's oral health on the developing foetus. The presented cardiovascular-oral health data base for the Balkan region can be used as a geographic, demographic and epidemiologic source of information for the detection and identification of new potential risk factors of individuals for preterm delivery and possible atherosclerosis development. Primary prevention of atherosclerosis should begin as early as possible, during pregnancy, in childhood, by creating a healthy way of life, which will be able to prevent or at least slow the development of atherosclerosis.

Conflict of Interest

None declared.

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MOGUĆI NOVI FAKTOR RIZIKA ZA PREMATURITET I KARDIOVASKULARNE BOLESTI U DJECE

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GRIT KIRSTEN-SARIĆ, SENAD SARIĆ, ANES JOGUNČIĆ, SAMIR PROHIĆ, AIDA RAMIĆ*

Parodontna bolest je kronična upalna, imunološki posredovana, bolest visoke učestalosti koja je povezana s aterosklerotskom kardiovaskularnom bolesti i mnogim sistemskim bolestima. Ako se parodontna bolest ne prepozna pravovremeno ili neadekvatno liječi, može dovesti do nastanka aterosklerotskih lezija i kliničke ekspresije aterosklerotske kardiovaskularne bolesti. Nedostatan uvid u moguće patološke implikacije statusa oralnog zdravlja u trudnica za nastanak ateroskleroze kao i prijevremenog poroda, inicirao je međunarodni znanstveno-istraživački projekt, koji se realizira u Bosni i Hercegovini, Republici Hrvatskoj i Njemačkoj, u periodu 2017.-2019./2020. godine, pod nazivom "Utjecaj oralnog zdravlja trudnica na kardiovaskularno zdravlje djece". Svrha projekta je evaluirati povezanost oralnog zdravlja s kardiovaskularnim zdravljem i općim zdravljem, uz osvrt na moguću pojavu prijevremenog poroda i rađanja djece niske porođajne mase. Istraživanje će utvrditi da li je trudnička parodontna bolest moguća novi faktor rizika za preuranjenu kardiovaskularnu bolest u djece. Također se želi ukazati na značaj pravilne higijene usne šupljine i redovitih stomatoloških pregleda trudnica u sprječavanju ili smanjenju pojave trudničke parodontne bolesti i utjecaja na komplikacije trudnoće i mogući preuranjeni kardiovaskularni rizik.

Deskriptori: RIZIK, ATROSKLEROZA, PREMATURITET

Uvod

Temeljnu ulogu u iniciranju, progresiji i komplikacijama kardiovaskularnih bolesti ima ateroskleroza koja se karakterizira suženjem lumena krvne žile zbog lokalnog zadebljanja unutrašnje stijenke krvne žile uslijed formiranja ateroskleroze (1). Jedan od temeljnih razloga što su bolesti uvjetovane aterosklerozom, i dalje jedan od vodećih uzroka obolijevanja i smrti diljem svijeta, je nedovoljno provođenje preventivnih aktivnosti (2, 3). Primarna prevencija ateroskleroze, koja treba početi još u trudnoći i ranoj dječjoj dobi, uključuje promicanje zdravog stila življenja (zdrava ishrana, izbjegavanje pušenja i izloženosti duhanom

dimu i primjerena tjelesna aktivnost) što će spriječiti ili odložiti nastanak faktora rizika za razvoj aterosklerotske bolesti. Sekundarna prevencija uključuje probr aterosklerotskih faktora rizika što omogućuje pravovremeno otkrivanje djece s povećanim rizikom za razvoj ateroskleroze kako bi se odgovarajućim preventivnim i terapijskim aktivnostima usporila ili odložila aterosklerotska bolest. S obzirom da ne postoji specifični lijek za aterosklerozu, najbolji način sprječavanja ateroskleroze i njenih komplikacija je edukacija i preventivne aktivnosti stanovništva (4).

Osim povezanosti oralnih bolesti sa sistemskim obolijevanjima, neki autori ukazuju na moguću poveznicu između parodontne bolesti u trudnica s rizikom prijevremenog poroda i rađanja djeteta niske porođajne mase kao i mogućom preuranjenom kardiovaskularnom bolesti u djece (1, 5-8). Cilj ovoga rada je evaluacija povezanosti oralnog zdravlja s kardiovaskularnom bolesti, prezentiranje utjecaja trudničke parodontne bolesti

na moguću prijevremeni porod i rađanje djeteta niske porođajne mase, utjecaja lošeg trudničkog oralnog zdravlja na pojavu faktora rizika za aterosklerozu u djece, kao i prikaza temeljnih aspekata aktualnog međunarodnog znanstveno-istraživačkog projekta pod nazivom "Utjecaj oralnog zdravlja trudnica na kardiovaskularno zdravlje djece".

Povezanost oralnog zdravlja s aterosklerotskom kardiovaskularnom bolesti

Oralne bolesti spadaju među najučestalije kronične nezarazne bolesti tokom cjelokupnog života (9). Oralno zdravlje, ključni je indikator blagostanja i kvalitete života, te je povezano s općim zdravljem (9, 10). Nepravovremeno dijagnosticirana i liječena parodontna bolest prelazi u kroničnu upalnu, imunološki posredovanu bolest karakteriziranu propadanjem parodontnog ligamenta i pripadajuće alveolarne kosti. Najznačajnije parodontopatogene bakterije (*Aggregatibacter actinomycetemcomitans*,

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Porphyromonas gingivialis, *Tannarella forsythia*, *Treponema denticola* i *Fusobacterium nucleatum*) nagomilavaju se u parodontnom džepu uzrokujući imunosni odgovor koji dovodi do oštećenja potpornih struktura i gubitka zuba (11). Povezanost oralnih bolesti i općeg zdravlja je složena i višestruka, tj. oralne bolesti imaju utjecaja na opće zdravlje, kao što i sistemske bolesti utječu na oralno zdravlje (9, 12, 13). Najveći broj oralnih bolesti dijele zajedničke faktore rizika, uključujući nezdravu prehranu bogatu šećerima, pušenje duhana i prekomjerna konzumacija alkohola, s kardiovaskularnim bolestima, zloćudnim tumorima, kroničnim bolestima dišnog sistema i dijabetes melitusom (9, 10).

Osim navedenih riziko faktora, smatra se da u nastanku parodontne bolesti značaj mogu imati i nasljedni faktori rizika. Znanstvenici smatraju da varijacije DNA sekvenci imaju učinak na individualni rizik za razvoj parodontne bolesti jer su utvrdili da uslijed varijacija genskih sekvenci može biti onemogućena aktivnost alfa defenzina, antimikrobnog peptida prisutnog u neutrofilnim granulocitima, odgovornih za uništenje parodontopatogenih bakterija (14). Munz M. i sur. otkrili su genske lokuse udružene sa sklonosti za agresivnu i kroničnu parodontnu bolest, gdje uslijed poremećaja u prirodnoj i stečenoj imunosti dolazi do parodontne bolesti (14). Najučestalije oralne bolesti, karies i parodontna bolest, mogu izazvati i pogoršati mnogobrojna sistemska oboljenja kao što su: infektivni endokarditis, miokarditis, koronarna srčana bolest, infarkt miokarda, cerebrovaskularna bolest, pneumonija, kronična opstruktivna bolest pluća, dijabetes melitus, komplikacija trudnoće (preeklampsija, mrtvorođenost i spontani pobačaj), rađanja djece prije termina i niske porođajne mase, osteoporozu, kronična bubrežna bolest i druga oboljenja (9, 12, 13, 15-17).

Aterosklerotska kardiovaskularna bolest spada među vodeće uzroke oboljevanja, prijevremene smrti i disabiliteta diljem svijeta. Osim nemodificirajućih, modificirajućih i netradijskih faktora rizika, smatra se da u nastanku ateroskleroze značaj može imati i kronična upala uvjetovana određenim mikroor-

ganizmima (18, 19). Njemački patolog Virchow (1948.), američki znanstvenik Ross (1986.) i švedski znanstvenik Hansson (2009.) smatraju da je ateroskleroza upalna bolest, tj. kronični upalni odgovor stijenke krvne žile na različite forme oštećenja endotela (20, 21). Mnogobrojna istraživanja ukazuju na povezanost parodontne bolesti i aterosklerotske kardiovaskularne bolesti (11, 22, 23). Povišene vrijednosti bioamarkera upale, C-reaktivnog proteina (CRP) faktora tumorske nekroze-alfa (TNF-alfa) i interleukina 6 (IL-6) kod pacijenata s udruženom parodontnom bolesti i aterosklerotskom kardiovaskularnom bolesti, ukazuju da je parodontna bolest mogući faktor rizika za aterosklerotsku kardiovaskularnu bolest (12). Sumarno govoreći, aterosklerotski proces uključuje dislipidemiju, endotelijalnu disfunkciju i permeabilnost i nakupljanje lipoproteina u intimi krvne žile (11).

Pojedinci s predominacijom *Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivialis*, *Tannarella forsythia* i *Treponema denticola* u zubnom plaku, imaju dva puta veću koncentraciju malih, gustih LDL-čestica (sd-LDL) i apolipoproteina B (apoB) u serumu vs. pojedinaца koji nemaju parodontnu bolest (11, 24). Endotelijalna disfunkcija temeljni je faktor u razvoju ateroskleroze, a disfunkcionalan endotel pokazuje protrombogeni, proinflamatorni i proaterogeni potencijal. Virulentne parodontopatogene bakterije produciraju lipopolisaharide koji stimuliraju Toll-like receptore (TLR) prisutne na endotelijalnim stanicama, a u daljnjem tijeku aterogeneze dolazi do povećanog nivoa endotelijalnih adhezijskih molekula i TNF-alfa (11). Endotelijalne adhezijske molekule privlače makrofage u subendotelijalni prostor, a zajedno sa TNF-alfa i parodontopatogenim bakterijama djelujući na mehanizme prirodne imunosti, povećavaju permeabilnost endotela (11, 12, 23). Veoma patogena bakterija *Aggregatibacter actinomycetemcomitans* uslijed proizvodnje toksičnog proteina leukotoksina (LtxA) može dovesti do endotelijalne apoptoze i povećanog broja endotelijalnih adhezijskih molekula promovirajući endotelijalnu permeabilnost (25).

Određene bakterije u zubnom plaku produciraju protein toplinskog šoka (HSP) koji uvjetuje stvaranje protutijela, te uslijed ukrštene rezistencije s endotelom, dolazi do endotelijalne disfunkcije, po tipu autoimune bolesti i iniciranja aterogeneze (23, 26). Disfunkcionalan endotel postaje permeabilan za lipoproteine i makrofage, trombocite i T- limfocite. Hemotaktični faktori iz endotelijalnih stanica i makrofaga induciraju nakupljanje većeg broja monocita koji fagocitiraju lipoproteine i pretvaraju se u pjenaste stanice, te se formira početna aterosklerotska lezija, masna pruga. Parodontopatogene bakterije zajedno s trombocitnim faktorom rasta (PDGF) i lipoproteinima induciraju migraciju glatkih mišićnih stanica, koje stvaraju gusti ekstracelularni matriks, iz medije u intimu krvne žile (11). Kronično upalno stanje uvjetovano parodontopatogenim bakterijama u interakciji s ostalim faktorima rizika uvjetovat će perzistiranje imunološko-inflamatornih procesa dovodeći do nastanka uznapredovalih aterosklerotskih lezija, tj. nastanka fibrolipidne nakupine (aterom) koji se sastoji od središnje lipidne jezgre koja je prekrivena fibroznom kapom. Ako se javi komplikacija plaka javit će se klinička simptomatologija aterosklerotske kardiovaskularne bolesti. Navedeno ukazuje na značaj preventivnih aktivnosti u očuvanju i unaprijeđenju oralnog zdravlja, a time i kardiovaskularnog i općeg zdravlja stanovništva.

Utjecaj parodontne bolesti na trudnoću

Povišena vrijednost cirkulirajućih gestacijskih hormona tijekom trudnoće uzrokuje visoku prevalenciju gingivitisa i hiperplazije gingive (27). Mnogobrojni autori navode moguću udruženost parodontne bolesti trudnica s rizikom prijevremenog poroda i rađanja djeteta niske porođajne mase (28-31). Smatra se da približno 40% trudnica ima određenu formu parodontne bolesti (16, 32). Trudnice sa parodontnom bolesti pokazuju 2-7 puta veću učestalost prijevremenog poroda (28, 33). Morre i sur. ukazuju da trudnice sa parodontnom bolesti su imale veliki broj fetalnih smrti (34). Istražujući povezanost parodontne bolesti trudnica i prijevremenih poroda Jeffcoat

i sur. utvrdili su da su umjereni ili teški oblik parodontne bolesti u ranoj trudnoći bili udruženi s prijevremenim porodom, neovisno o drugim poznatim faktorima rizika za prijevremeni porod (35).

Virulentne parodontopatogene gram - negativne anaerobne bakterije prisutne u zubnom plaku proizvode lipopolisaharide, djeluju kao endotoksini, kao i drugi toksični produkti koji uzrokuju povišene vrijednosti markera upale poput: interleukina (IL-6, IL-8 i IL-1b), TNF-alfa i prostaglandina E_2 (PGE $_2$), koji cirkulacijom dopijevaju do maternice i posteljice dovodeći do komplikacija trudnoće (spontani pobačaj i mrtvorodenost) kao i prijevremenog poroda i rađanja djece niske porođajne mase (32, 35, 36). Majke prijevremeno rođene djece ili djece niske porođajne mase imale su značajno povišenu vrijednost PGE $_2$ u gingivalnoj tekućini vs. majkama terminski rođene djece ili djece poželjne porođajne mase (36).

Osim parodontne bolesti tokom trudnoće može se javiti i veća prevalencija karijesa što je uvjetovano smanjenim pH usne šupljine, izraženijim konzumiranjem rafiniranih šećera i neprimjerenom oralne higijene (37). Smatra se da virulentne parodontopatogene gram-negativne anaerobne bakterije, kao i kod parodontne bolesti, mogu produciranjem IL-1b, TNF-alfa i PGE $_2$ dovesti do prijevremenog poroda i rađanja djece niske porođajne mase kod trudnica s težim oblicima karijesa (32, 35). Uzroci prijevremenog poroda u više od 50% slučajeva nisu poznati, a kao mogući uzroci između ostaloga, navode se socioekonomski faktori, akutna i kronična oboljenja majki, višeplođna trudnoća, porođičarski uzroci, nasljedna oboljenja i placentalni uzroci (38).

Bitno je utvrditi moguće faktore rizika za prijevremeni porod i rađanja djece niske porođajne mase jer je na taj način moguće znatno smanjiti učestalost prijevremenog poroda i rađanja djece niske porođajne mase, čime se smanjuje stopa perinatalne smrtnosti i moguće perinatalne komplikacije. Prijevremeno rođena djeca i novorođenčad niske porođajne mase imaju veću učestalost faktora rizika za kardiovaskularnu bolest vs. terminski rođenoj djeci i djeci poželjne

porođajne mase (39). Povišena vrijednost glukokortikoida tijekom intrauterinog perioda uvjetuje u postnatalnom periodu programiranje osovine hipotalamus-hipofiza-nadbubrežna žlijezda što ima temeljnu ulogu u većoj učestalosti faktora rizika za kardiovaskularne bolesti u prijevremeno rođene djece i djece niske porođajne mase vs. terminski rođenoj djeci i djeci poželjne porođajne mase (40).

Smatramo da se u svakodnevnom praktičnom radu nedovoljno provodi probr statusa oralnog zdravlja trudnica. Probirom statusa oralnog zdravlja mogli bi se pravovremeno procijeniti održavanje oralne higijene i identificirati trudnice koje imaju karijes ili parodontnu bolest. Pravovremenim stomatološkim liječenjem može se smanjiti učestalost oralnih bolesti kod trudnica, a u kontekstu gore navedenih razmatranja, mogla bi se smanjiti učestalost prijevremenog poroda i rađanja djece niske porođajne mase. te spriječiti ili smanjiti preuranjeno ispoljavanja faktora za aterosklerotiku kardiovaskularnu bolest.

Znanstveno-Istraživački projekt:
"Utjecaj oralnog zdravlja trudnica na kardiovaskularno zdravlje djece"

S obzirom na to da trudnice i liječnici nedovoljno pažnje posvećuju oralnom zdravlju trudnica, kao i da je nedostatno znanje o utjecaju neprimjerenog oralnog zdravlja trudnica na tijek trudnoće i moguću preuranjenu pojavu rizika za aterosklerotiku kardiovaskularnu bolest, iniciran je međunarodni znanstveno-istraživački projekt, pod nazivom "Utjecaj oralnog zdravlja trudnica na kardiovaskularno zdravlje djece". Aktualno kohortno istraživanje (prva faza istraživanja završena, druga faza u tijeku) se realizira u Bosni i Hercegovini, Republici Hrvatskoj i Njemačkoj, tijekom 2017-2019./2020. godine. Između ostalog, ciljevi ovog istraživanja su: utvrditi da li trudnička parodontna bolest utječe na gestacijsku dob i porođajnu masu djece, kardiovaskularno zdravlje dojenčadi i male djece, utvrditi da li je trudnička parodontna bolest faktor rizika za aterosklerotiku kardiovaskularnu bolest, kao i da li predškolska djeca čije su majke imale trudničku parodontnu bolest imaju

izraženije prediktore prijevremenog kardiovaskularnog rizika (povećan indeks tjelesne mase, viša vrijednost krvnog tlaka i zadebljanje kompleksa intima-media karotidnih arterija) vs. djeci čije su majke imale primjereno trudničko oralno zdravlje (4).

U istraživanje su uključene majke i djeca isključivo urednog zdravstvenog stanja. Tokom regularnih pregleda trudnica, prvi odnosno drugi ili treći trimestar trudnoće, stomatološkim pregledom utvrđeno je oralno zdravlje trudnica. Uključujući opći pedijatrijski pregled i stomatološki pregled, skupina djece bit će praćena do njihove treće odnosno četvrte godine života (4). Djeca će biti klasificirana prema njihovoj gestacijskoj starosti i porođajnoj masi, a bit će im određen krvni tlak, ultrazvučnim pregledom procijenjena debljina kompleksa intima-media karotidne arterije, a ehokardiografskim pregledom utvrđen hemodinamski status djece (4). Uptinicima su analizirane životne navike i primjerenost oralne higijene majki i djece.

Smatramo da će istraživanje utvrditi da određeni broj majki uslijed nezdravih životnih navika, nepravilne oralne higijene i nedovoljnih posjeta stomatologu ima parodontnu bolest, kao i da rađaju djecu niže gestacijske dobi i niske porođajne mase sa svim svojim mogućim komplikacijama, što bi smanjilo financijske troškove neonatalne intenzivne njege i terapije kao i kardiovaskularne reperekusije zdravlja novorođenčeta. Određena skupina djece s nižom gestacijskom dobí starosti i niskom porođajnom masom će u dobi od tri ili četiri godine imati veći indeks tjelesne mase, veću vrijednost sistoličkog i dijastoličkog krvnog tlaka i veću debljinu kompleksa intima - media karotidne arterije vs. poželjnim vrijednostima indeksa tjelesne mase, krvnog tlaka i debljine kompleksa intima-media karotidne arterije kod djece rođene u terminu i poželjne porođajne mase.

Preliminarni rezultati Prve faze Projekta (period: 2017-18.) su: prosječna dob 43 trudnice je $30,7 \pm 5,7$ godina; 90,7% trudnoća protječe uredno; komplikacije su uočene u 9,3%. Tijekom trudnoće kod 86,05% trudnica nije dijagnosticirana nova bolest. Rijetku/laku bolest imalo je

9,3% trudnica, 4,65% je imalo teže komplikacije. Edukacijski status: završena Visoka Škola 8 (18,60%), Srednja Škola: 4 (9,30%), Sveučilišno obrazovanje: 31 (72,10%) trudnica. Navike u prehrani: 49% majki konzumira mliječne proizvode dnevno; voće 65%: dva ili više puta dnevno; povrće 23%: dva ili više puta dnevno; meso 51%: dnevno; 14% konzumira meso nekoliko puta sedmično; riba 46%: jedan put sedmično; 26% rijetko ili nikada. KEP (Cavities/Tooth extraction/seal) index: $12,32 \pm 5,7$; plak index 0,312; popravljani zubi 65,62%; kariozni zubi 12,5%. Ovi rezultati indiciraju svjesnost trudnica o značaju oralnog zdravlja i njegovog utjecaja na razvoj djeteta. Međutim, neophodno je pričekati kraj studije i definitivne rezultate. Prezentirana kardiovaskularna-oralna zdravstvena baba podataka za Balkansku regiju može se primijeniti kao i geografski, demografski i epidemiološki izvor informacija za detekciju i identifikaciju mogućih novih faktora rizika za prematuritet i razvoj ateroskleroze.

Zaključak

Mnogobrojna istraživanja ukazuju da virulentne parodontopatogene bakterije prisutne u zubnom plaku uslijed perzistiranja kroničnog upalnog procesa mogu biti faktor rizika za aterosklerotiku kardiovaskularnu bolest i negativno utjecati na sistemsko zdravlje pojedinca. Trudnička parodontna bolest, nepravovremeno dijagnosticirana i neliječena, kao mogući novi faktor rizika za kardiovaskularnu bolest, može nepovoljno utjecati na tijek trudnoće, tj. trudnoća može rezultirati rađanjem djece prije termina i niske porođajne mase, koja u kasnijoj dobi mogu imati preuranjene prediktore kardiovaskularne bolesti. Primarna prevencija aterosklerotičke kardiovaskularne bolesti treba početi još tijekom trudnoće. Adekvatna prenatalna njega treba uključiti i zaštitu trudničkog oralnog zdravlja koja treba biti temeljena na pravilnoj higijeni usne šupljine i redovitim stomatološkim pregledima, što će spriječiti ili smanjiti učestalost pojave trudničke parodontne bolesti i njenog utjecaja na komplikacije trudnoće i moguću preuranjenu kardiovaskularnu rizik.

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Nije potrebno/None

SUKOB INTERESA/CONFLICT OF INTEREST

Autori su popunili the *Unified Competing Interest form* na www.icmje.org/coi_disclosure.pdf (dostupno na zahtjev) obrazac i izjavljuju: nemaju potporu niti jedne organizacije za objavljeni rad; nemaju financijsku potporu niti jedne organizacije koja bi mogla imati interes za objavu ovog rada u posljednje 3 godine; nemaju drugih veza ili aktivnosti koje bi mogle utjecati na objavljeni rad./ *All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: no support from any organization for the submitted work; no financial relationships with any organizations that might have an interest in the submitted work in the previous 3 years; no other relationships or activities that could appear to have influenced the submitted work.*

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Summary

A NEW POTENTIAL RISK FACTOR FOR PREMATURITY AND CARDIOVASCULAR DISEASES IN CHILDREN

Senka Meshović-Dinarević, Lutvo Sporišević, Berislav Topić, Vjekoslav Krželj, Sanja Jurišić, Grit Kirsten-Sarić, Senad Sarić, Anes Jogunčić, Samir Prohić, Aida Ramić

Periodontal disease is a chronic inflammatory, immune mediated, high-frequency disease associated with atherosclerotic cardiovascular disease and many systemic diseases. If the periodontal disease is not detected promptly, or inadequately treated, can lead to the formation of atherosclerotic lesions and the clinical expression of atherosclerotic cardiovascular disease. Insufficient insight into the possible pathologic implications of the oral health status in pregnant women for the development of atherosclerosis and premature birth, initiated an international scientific research Project, which is being implemented in Bosnia and Herzegovina, Croatia and Germany in the period 2017-2019/2020, entitled "The impact of oral health of pregnant women on the cardiovascular health of children". The purpose of the Project is to evaluate the relationship of oral health and cardiovascular health and general health, with reference to the possible occurrence of premature birth and the birth of children of low birth weight. The research will determine whether the maternity periodontal disease is a possible new risk factor for premature cardiovascular disease in children. It also wants to highlight the importance of proper oral hygiene and regular dental examinations of pregnant women in preventing or reducing the incidence of maternity periodontal disease and the impact on pregnancy complications and possible premature cardiovascular risk.

Descriptors: RISK, ATHEROSCLEROSIS, PREMATURITY

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The Oral Health of Pregnant Women as a New Potential Risk Factor for Prematurity and Cardiovascular Diseases in Children

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Pregnancy is a state in which complex physical and physiological changes are present, these have important effects on multiple organ systems. Some authors pointed out the possible connection between periodontal disease in pregnant women with the risk of preterm delivery, newborns of a low gestational age with low birth masses and possible cardiovascular disease. Cardiovascular disease atherosclerosis is now one of the leading causes of death in developed countries, it begins in childhood, and goes a long time without manifesting symptoms, increasing with age, it begins to seriously threaten health. Insufficient insight into the possible pathological implications of the oral health status of pregnant women with the premature expression of cardiovascular risk factors in children, initiated this research. The aim of the study is to investigate more prominent predictors of early cardiovascular risk factors: increased body mass index, high values of blood pressure and the thickening of the intima-media carotids complex in comparison to children whose mothers had good oral health during pregnancy. Regular dental therapy/care can decrease the frequency of the occurrence of caries and periodontal disease in pregnant women, the frequency of prematurity and low birth weight with all its potential complications, decreasing the financial costs of neonatal intensive care management and the cardiovascular repercussions on newborn's health. Primary prevention of atherosclerosis should begin as early as possible, during pregnancy, in childhood, creating a healthy way of life, which will be able to prevent or at least slow the development of atherosclerosis.

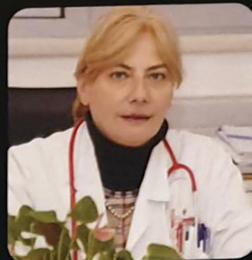
Biography

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Joint Event on Nursing Diagnosis, Parasitology & Pediatric Cardiology

December 05-06, 2019, Florence, Italy

THE INFLUENCE OF MOTHER'S NUTRITION AND ORAL HEALTH ON THE CHILD'S BLOOD VESSEL DEVELOPMENT

Introduction: The correlation of oral health and cardiovascular diseases has been evaluated in the past, but not the influence of mother's nutrition, its oral health on cardiovascular foetal system development, which can lead to a slower foetus development, lower birth weight, as well as differences in blood vessels development.

Aim: The aim of our study was to evaluate the relationship between oral health of mothers, dietary habits during pregnancy with the development of the coronary and carotid arteries.

Patients & Methods: The study included 40 pregnant women and their newborns. During pregnancy the dental mother's status and eating habits were analysed. After delivery a detailed colour Doppler echocardiography including carotid vessels has been performed.

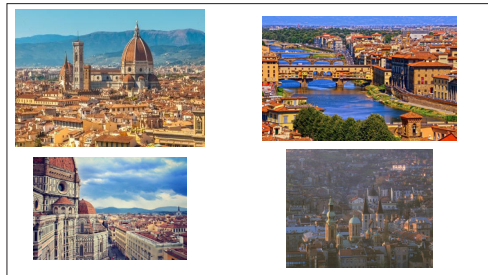
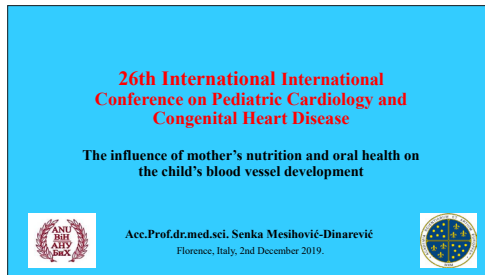
Results: There was a significant correlation of LVEDs and mothers eating habits ($\rho = -0.415$, $p = 0.044$), whereby a better value LVEDs determined in infants whose mothers had worse eating habits. Carotid Intima Media had moderate connection with nutrition intake on both of the carotids, whereby the thicker intima had a pregnant woman with poor eating habits ($\rho = -0.492$, $p = 0.03$). Fortified is a significant correlation between the diameter of the right coronary artery and the KEP index, where the pregnant woman had better diameters with the smaller blood KEP index ($\rho = -0.693$, $p = 0.047$). Diameter of descending aorta had a significant association with the dietary habits, and larger diameters defined in the infants, whose mothers had worse eating habits ($\rho = -0.508$, $p = 0.011$). Ejection fraction (EF) has a significant correlation with the KEP index values ($\rho = 0.507$, $p = 0.014$). In mothers with KEP index <10, EF had significant lower values ($p = 0.002$).

Conclusion: There was a significant connection between diet and oral health status of mothers with some segments of the development of cardiovascular system in infants. It is necessary to extend the study and test inference on a larger sample.

Biography

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The influence of mother's nutrition and oral health on the child's blood vessel development

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Introduction

The correlation of oral health and cardiovascular diseases has been evaluated in the past, but not the influence of mother's nutrition, its oral health on cardiovascular foetal system development, which can lead to

- a slower foetus development,
- lower birth weight,
- as well as differences in blood vessels development.

Pregnancy is a state in which complex physical and physiological changes are present, these have important effects on multiple organ systems.

Some authors pointed out the possible connection between periodontal disease in pregnant women with

- the risk of preterm delivery,
- newborns of a low gestational age with low birth masses and
- possible cardiovascular disease.

The aim of our study

- is to evaluate the relationship between
- oral health of mothers,
- dietary habits during pregnancy with
- the development of the coronary and carotid arteries, the cardiovascular system.

Topics:

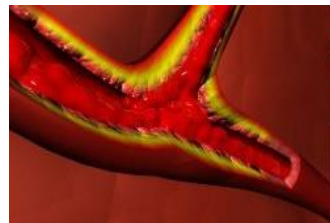
- Atherosclerosis
- Risk factors
- Oral health
- Pregnancy
- Prematurity
- Research data
- Conclusiones

Topic:

Atherosclerosis

Cardiovascular disease Atherosclerosis is now one of the leading causes of death in developed countries, it begins in childhood, and goes a long time without manifesting symptoms, increasing with age, it begins to seriously threaten health.

Atherosclerosis /the most frequent disease of the arteries/ is characterized by lumen reduction of blood vessels due to local thickening of internal blood vessels caused by plaque /atheroma.



As a cardiovascular disease, **atherosclerosis is an interdisciplinary problem, multifactorial in its etiopathogenesis, course and repercussions,** demands **the action of:**

- family doctors,
- physicians,
- paediatricians,
- cardiologist,
- paediatric cardiologist,
- neurologist,

- diabetologist,
- endocrinologist,
- cardiac and vascular surgeons,
- neurosurgeon,
- radiologist,
- specialist of nuclear medicine,
- epidemiologist,
- nutritionist,
- pathologist,
- biochemist.

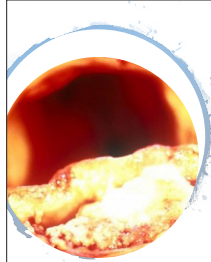
with the aim of **early detection and treatment of atherosclerosis** as well as the **reduction of development of risk factors for coronary artery diseases.**

- **Pathophysiology** of the disease is to damage cells that line the inner surface of the arteries that endothelium due to **chemical** or **mechanical** damage.

- **Elevated blood cholesterol, smoking, or elevated homocysteine** (now one of the more investigated the causes of atherosclerosis) are examples of **chemical** damage and
- **mechanical** damage to the cells are: **high blood pressure, damage of the catheter during diagnostic procedures or even infections.**

- As the **first stage of development of atherosclerosis** occurs **"fatty streak."**

- It is totally **reversible**, which means that the **cessation of the activities of harmful pathogens, endothelial cells recover completely.**
- However, if **exposure to adverse event continues**, atherosclerotic plaque **grows and more narrow lumen.**
- Consequently, **reducing blood flow and tissue oxygen supply becomes insufficient.**



- **In the blood vessel** itself due to reduced elasticity, an **increase of blood pressure** occurs.
- **Elevated blood pressure** can lead to: cracking in blood of the coat or its stratification with the formation of aneurysms or plaque, which can calcify and slim down the wall of the vessel with the ability of forming a clot.
- For atherosclerotic disease itself **plaque composition** rather than its size is **much more important.**

- **Early precursors of vascular changes – subclinical atherosclerosis** – warrant special attention as this process **can be stabilized or even reversed if treated in time.**

- Sonographic Intima Media Thickness measurement of the carotid artery (cIMT: carotid Intima-Media-Thickness) is considered **a valid surrogate marker for cardiovascular risk** allowing assessment of atherosclerotic changes at a very early stage.



Topic:

Risk factors

The most important **risk factors** for the **development of atherosclerotic disease** are:

- hyperlipidemia,
- hypertension,
- smoking,
- diabetes, high fibrinogen, a male sex at younger and middle age,
- menopause in women taking oral contraceptives or hormone replacement therapy only with presence of other risk factors,
- excessive weight, increased level of homocysteine,
- physical inactivity, heredity and immune response in some diseases.

- **The primary intention of prevention** is to **preclude the occurrence of risk factors** for atherosclerosis.

- **The secondary** is **to prevent the development or aggravation of the illness** along with the **reduction or control of existing risks.**

- **Primary prevention should begin as early as possible**, during pregnancy, in childhood, creating a healthy diet, eliminating smoking, regular physical activity, which will prevent or at least slow the development of atherosclerosis.

The consequences of atherosclerosis are:

coronary or ischemic heart disease,

myocardial infarction,

cerebrovascular disease and cerebrovascular accident (80% of all heart attacks and brain due to atherosclerosis),

narrowing or blockage of peripheral arteries, carotid arteries,

particularly the legs, which can lead even to the development of gangrene

Since
there is no specific cure for atherosclerosis,
the **best way to prevent this disease,**
is **prevention!**

Therefore,
it is necessary to establish
a **dialogue in cardiovascular medicine!**

Topic:

Oral health

The association of oral health with atherosclerotic cardiovascular diseases

- Oral diseases are among the most common chronic non-communicable diseases during the entire life.
- Oral health is a key indicator of well-being and quality of life, and is closely connected with the general health.
- The non-diagnosed and treated periodontal disease becomes a chronic inflammatory, immune-mediated disease characterized by deterioration of the periodontal ligament and associated alveolar bone.
- Correlation between oral diseases and general health is complex and multifaceted.

The largest number of oral diseases share common risk factors, including unhealthy diet high in sugar, tobacco smoking and excessive alcohol consumption, with cardiovascular disease, malignant tumors, chronic diseases of the respiratory system and diabetes mellitus.

The oral cavity is an integral part of the human organism and therefore there exists a great connection between oral health and systemic health. Not only do some systemic diseases such as

- diabetes,
- osteoporosis,
- HIV infection,
- trisomy 21

have a predisposition for periodontitis but an opposite applies.

Susceptibility to certain systemic disease is higher in patients with periodontitis than in healthy people:

- chronic periodontitis is a risk factor for future cardiovascular disease,
- pregnant women with chronic periodontitis have more frequent preterm birth and
- newborns have a low birth weight.

- The explanation for the pathophysiological mechanisms of paradont focus and systemic disease is associated with elevated levels of circulating pro-inflammatory cytokines and prostaglandins derived from:

- diseased paradont,
- gram negative bacteria and their endotoxin-like substances,
- that appear from subgingival biofilms immediately entering the bloodstream.



The dominant problems of everyday dental practice are: caries, periodontal disease, occlusal abnormalities, the relationship of oral and general health and a holistic approach to the patient.



Caries and periodontal disease are of an infectious etiology therefore the prevention of dental caries and periodontal disease means preventing odontogenic foci.



A Periodontal pocket is a risk factor for the development or worsening of systemic focal disease, because the infection is always present in it; a pocket flora is various, massive, virulent and penetrates the soft wall of the pocket, the pocket is under constant mechanical stimulation during chewing, swallowing and speaking, all of which favor the penetration of bacteria into circulation and the formation of transient bacteremia.



Interdisciplinary cooperation in the elimination of potential negative effects of periodontal infections will result in better systemic health.

Dental caries and periodontal disease are the most common and significant oral disease, they can cause and aggravate numerous other disease:

- of the **cardiovascular system** (infective endocarditis, atherosclerosis, myocarditis and myocardial infarction),
- of the **respiratory system** (pneumonia, chronic obstructive pulmonary disease, bronchial asthma and pulmonary abscess),
- **neurological disorders** (cerebral infarction and cerebral abscess),
- **diabetes mellitus, rheumatoid arthritis,**
- **Alzheimer's disease,**
- **complications of pregnancy** (preeclampsia, stillbirth, miscarriage),
- **preterm births and low birth weight, osteoporosis.**

Topic:

Pregnancy

- **Pregnancy** is a state in which there are complex physical and physiological changes, which have important effects on multiple systems of organs. **High levels of circulating estrogen during pregnancy** are associated with high incidence of gingivitis and gingival hyperplasia or certain forms of periodontal disease. It is believed that approximately **40% of pregnant women** have a certain form of periodontal disease.
- Offenbacher et al. (1996) first suggested a **possible link between periodontal disease and risks for child delivery of a low gestational age or small birth weight**. Many researchers suggest a possible link between periodontal disease in pregnant women with a risk for preterm delivery, respectively, the birth of babies with low birth weight.
- Researches show that **in pregnant women with periodontal disease there is a 2-7 times higher risk for prematurity.**

- That is why dentists need to **motivate, educate and instruct** pregnant women towards a **higher level of oral hygiene** and to repair all dental lesions in **dental therapeutic procedures**, especially **periodontal pockets**, thereby **reducing the number of premature births.**

It is considered that **in the development of periodontal disease a hereditary risk factors** could have the importance.

Scientists believe that **DNA sequences variations** have an effect on the individual risk for the development of periodontal disease because they have found that **due to the variation of gene sequences**, the activity of alpha defensins (antimicrobial peptides present in neutrophil granulocytes/ which is responsible for the destruction of periodontopathogenic bacteria, could be disabled).

Munz et al. have discovered the **genetic** associated with susceptibility for chronic and aggressive periodontal disease where due to disorders in congenital and acquired immunity leads to development of periodontal disease.

Topic:

Prematurity

The incidence of births of premature infants and newborns of a small birth weight is between **5-18%**, depending on the geographical area and population characteristics.

The causes of preterm birth in more than **50%** of cases are not known, and as possible causes, among other things, are cited:

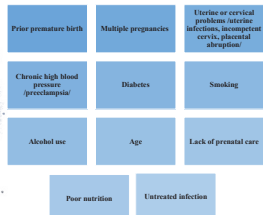
- a socioeconomic factors,
- acute and chronic diseases of mothers,
- multiple pregnancy,
- obstetrical causes,
- hereditary diseases and
- placental causes.



- It is important to **identify possible risk factors for preterm birth and birth of children of low birth weight** because in that way is possible to **significantly reduce the incidence of premature birth and the birth of children of low birth weight**, which **decrease the rate of perinatal mortality and possible perinatal complications.**

- Preterm children and infants of low birth weight have a **higher incidence of risk factors for cardiovascular disease** vs. **term infants** and children of desirable birth weight.

Risk factors for prematurity



It was established that the mothers who had given birth to **premature infants or children of a small birth weight** had **significantly elevated levels of PGE2 in the gingival fluid** opposed to the mothers who had given birth to children in the dedicated time or children with an appropriate birth weight.

During pregnancy, there is an **increased susceptibility to caries** due to:

- the **increased acidity of the oral cavity,**
- the **increased consumption of refined sugars and**
- **poor oral hygiene.**

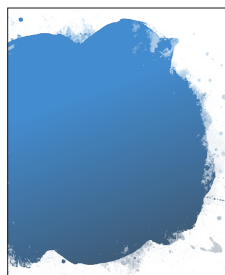
- Caries bacteria in children are usually transmitted by direct transmission through the mother's saliva.
- Mothers with high titers of *Streptococcus mutans* in their saliva are going to substantially transmit the bacteria to their baby – by vertical transmission, creating conditions for early childhood caries.
- Of course, the time and frequency of the transmission of bacteria, the child's preference for the accumulation of bacteria on its teeth, the composition and flow of the child's saliva, the amount of refined sugar in the baby's food, are all significant predictors of early children's caries.

Due to the immaturity of their organ systems, premature babies and infants of a small birth weight are **among in vulnerable group of infants** - complications due to prematurity are the leading cause of death in children under 5 years of age.

- Preterm children or infants of a small birth weight exhibit a **higher incidence of cardiovascular risk factors** (obesity, hypertension, dyslipidemia), and type 2 diabetes mellitus.
- Animal and epidemiological studies indicate that conditions of elevated levels of glucocorticoids intrauterine during life, programme the hypothalamus-pituitary-adrenal gland axis that plays a **key role in the higher incidence of cardiovascular risk in premature infants and children of a small birth weight.**

- Apart from the **role of microbiome mouth** (microbiome - all microbes, their genome and mutual interaction in a particular environment) as a **risk factor** for premature delivery or the birth of newborn of small birth weight, it is possible that the **microorganisms of the oral cavity** condition chronic inflammation that can represent an **atherosclerotic cardiovascular risk factor.**

- Adequate prenatal care should include **oral health care of pregnant women**, i.e. for pregnant women, there is a need to point out the **importance of practicing regular oral hygiene and the need for periodic or as many as or as frequently as needed dental checkups.** Any dental intervention or dental radiography is most appropriate to be undergone in a dental practice **upon the completion of organogenesis**, i.e. **in II or III trimester of pregnancy.**

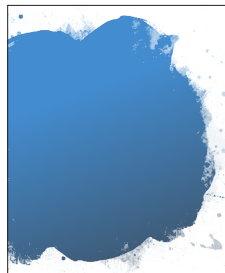


A significant number of pregnant women maintain inappropriate oral health.

- Insufficient visits to the dentist,
- inappropriate oral hygiene and
- the consumption of unhealthy food,

all affect the appearance of **caries as well as parodontal disease** in pregnant women.

- The sufficient screening/screening of oral health status of pregnant women **is not carried out in daily work**, so with screening status of oral health in a greater number of pregnant women, including the assessment of oral hygiene, we would be able to timely identify pregnant women who have **dental caries** respectively **periodontal disease.**
- With **timely dental treatment** we could **reduce the incidence of dental caries and periodontal disease** in pregnant women, and **may reduce the incidence of preterm delivery and the birth of newborns of a small birth weight, an early childhood caries and predictors of early atherosclerotic cardiovascular risk** (increased body mass index, blood pressure and thickening of the carotid intima-media complex).



In a cohort of children, who are preterm or have a low birth weight,

- a certain number of children age 3 have a greater body mass index,
- a higher value of systolic and diastolic blood pressure, as well as
- a thickening of the intima-media complex of the carotid artery with
- incipient signs of cardiovascular system disease.

Insufficient insight into the possible pathological implications of the oral health status of pregnant women, their eating habits with the premature expression of cardiovascular risk factors in children, initiated this research.

Topic:

Research data

PROJECT

- "Cardiovascular Disease and Oral Health - The impact of oral health of pregnant women on the cardiovascular health of children" a **Project** that is run by the Committee of the Cardiovascular Disease Department of Medical Sciences ASA of Bosnia and Herzegovina, during 2017, the first phase of research was completed according to plan /12 months / as well as second phase /2017-2019/.
- In this study **43 pregnant women from Bosnia and Herzegovina and Croatia** were included, with a plan to also include pregnant women from Slovenia.

An assessment of



The Project's common goals are to give answers to:

- Does and in what capacity **the oral health of pregnant women influence pregnancy?**
- Does **insufficient oral health of pregnant women** (periodontal disease and certain forms of caries) **influence gestational age, birth mass of children or oral, and cardiovascular health of newborn's, infants and small children?**
- **Is chronic inflammation of the oral cavity** (periodontal disease and caries) in pregnant women **a atherosclerotic and cardiovascular risk factor**, that is; do preschool children whose mothers during pregnancy had periodontal disease and/or caries, have a more prominent predictor of early cardiovascular risk (increased body mass index, high value of blood pressure and thickening of intima-media carotids complex) in comparison to children whose mothers during pregnancy had good oral health?

To achieve these goals, we are conducting **the research that can last up to 48 months**, using a multidisciplinary approach which includes:

- a gynaecologist,
- a dentist,
- a paediatrician,
- a radiologist,
- a cardiologist,
- nutritionists,
- epidemiologists and
- statistics

These examinations integrated research from 3 respected centres in B&H and Croatia using combined experience and skills.

The aim of this research is to investigate **more prominent predictors of early cardiovascular risk**

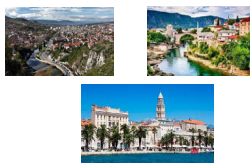
- **increased body mass index,**
- **high values of blood pressure and**
- **the thickening of the intima-media carotids complex**

in **comparison** to children whose mothers had **good oral health** during pregnancy.

These are the results of the **First and Second phase of the Project** within the Southeastern European region: „Cardiovascular disease and Oral health – the influence of pregnant women's oral health on children's cardiovascular health“ conducted in: **Sarajevo, Mostar, Split.**

The plan is to the finish project:

- **2020 III phase.**



Respondents

- The survey is designed as a **kohort study**: include **mothers /pregnant women** selected by random selection (randomized sampling).
- During **regular gynecological and obstetric-examination** (being I trimester, if necessary, II and III trimester of gestation) a **suggestion** was given to pregnant women to **do their dental examination in order** to assess their **oral health status**.

- The **general health status** of the **pregnant women** was determined on the basis of an assessment of their **medical records**.

The research **did not include**:

- **pregnant women with cardiovascular diseases,**
- **diabetes mellitus,**
- **kidney disease or any chronic illnesses.**

The survey testing assesses the **habits of pregnant women**:

- **eating habits,**
- **physical activity,**
- **alcohol consumption,**
- **drugs and smoking.**

II phase:

The children **were evaluated**

- **as newborns,**
- **preterm infants,**
- **newborns of a desirable body weight and**
- **newborn of a small birth weight,**

they would be followed up to **their third or fourth year of life.**

During the systematic review (the first month of life, the first year, the third and fourth year of life) **pediatricians evaluate:**

- the basic characteristics related to pregnancy and childbirth,
- analysis of the eating habits of children,
- anthropometric parameters,
- determine blood pressure values and
- while radiologists determine the value of complex intima-media carotid artery
- a cardiologist by echocardiography evaluate the hemodynamic status of the respondents.

- The study included children of proper health conditions, i.e. children with congenital anomalies or certain chronic illnesses were excluded from the study.
- Dentists judged the status of dental health of pregnant women and children, and evaluate the appropriateness of the oral health of pregnant women and children.
- The research is based on the principles of the Helsinki Declaration from 1975 and its amendments in 2008.



In order to implement the principles of ethical and bioethical research a consent / approval of the appropriate ethics committees / commissions was obtained.



Voluntary inclusion of pregnant women and children is confirmed by signing an informed consent form.

Research Methods

After signing the informed consent form i.e. informing mothers /pregnant women, by research methodology the following tests are conducted /I phase/ :

- survey testing
- dental examination.

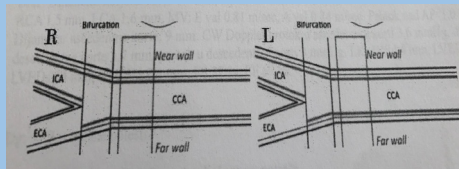
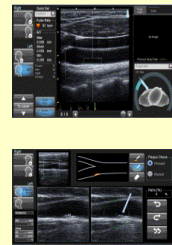
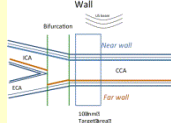
In II phase the following examination of Children was performed:

- survey testing,
- anthropometric measurements,
- determination of blood pressure,
- dental examination,

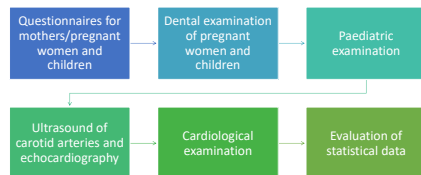
- determination of thickness of intima-media complex of the carotid blood vessels by two-dimensional Color Doppler ultrasonography,
- two-dimensional Color Doppler echocardiographic evaluation of the cardiovascular system.



Ultrasound Pattern of Near and Far Wall



Methods



Survey sheets were originally designed, they include questions about their habits in food intake (frequency, quantity and types) and fluids, and the frequency and intensity of physical activity.

Questionary for mothers:

Questionary of dental status in mothers:

Childs Questionary:

Anonymous Questionnaire for gynaecologists and dentists:

- As a dentist I avoid the application of local anaesthesia with adrenalin to pregnant women during all months of pregnancy?
- I avoid any kind of X raying pregnant women?
- In pregnancy the extraction of a tooth under pain is not recommended?
- I avoid therapy of gravidity gingivitis in pregnant women in all phases of pregnancy?
- Trepanation of teeth, the cause of acute dentogen infection, and incisions are not recommended in pregnant women?

The Study Workflow:

Pregnant women-gynecologist-dentist-
radiologist- cardiologist-epidemiologist

Patients and methods:

The study included 43 pregnant women and their newborns / I phase/

During pregnancy the dental mother's status and eating habits were analysed

After delivery a detailed colour Doppler echocardiography including carotid vessels has been performed

Preliminary study data I phase /2017-2018/:

- mean age of 43 pregnant women is 30.7+/-5.7 years,
- 90.3% pregnancy ran properly,
- complication detected in 9,7%

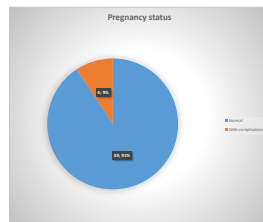
Preliminary study data II phase /2018-2019/:

Included: **40 children** due to sufficient obtained research data

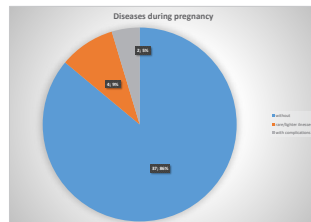
- Echocardiography
- Color Doppler of carotid arteries

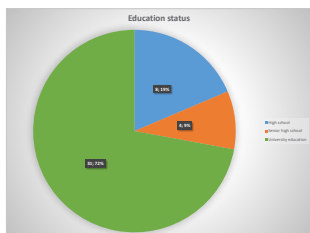
Table 1. Demographic characteristics

	n	%
AGE		30.7 ± 5.7
PREGNANCY STATUS		
NORMAL	39 (90.70%)	
WITH COMPLICATIONS	4 (9.30%)	
EDUCATION STATUS		
HIGH SCHOOL	8 (19.05%)	
SENIOR HIGH SCHOOL	4 (9.52%)	
UNIVERSITY EDUCATION	31 (71.43%)	
DISEASES DURING PREGNANCY		
WITHOUT	37 (92.45%)	
ARTE RIOPATHY, HYPERTENSION	2 (4.76%)	
WITH COMPLICATIONS	3 (7.35%)	



- During pregnancy, **87.1%** mothers had no new disease diagnosed.



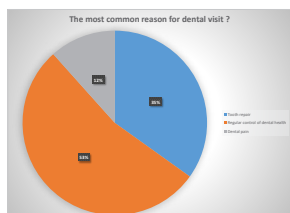
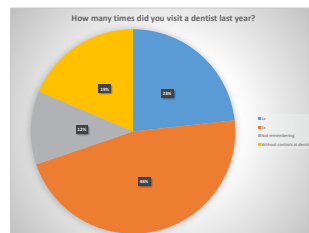
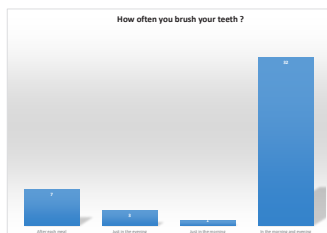
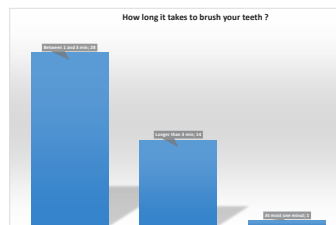
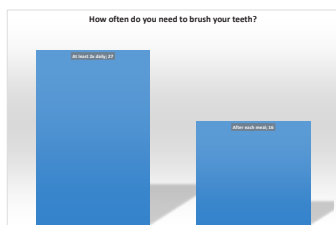


Eating habits

dairy products 48.4% : daily,
 fruit 64.5% : two or more times per day,
 vegetables 22.6% : two or more times per day,
 meat 41.9% : daily; meat in 45.2% few times during week
 fish in 35.2%: once a week; in 35.8% rarely or never

- Only 3.2% of women in pregnancy consumed **Alcohol** and 3.7% of respondents consumed **cigarettes**.

Assessment of oral hygiene



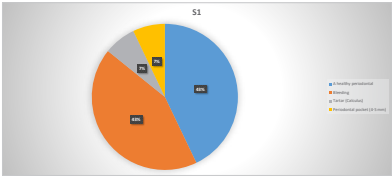
Dental status

KEP (Cavities/Tooth extraction/seal) index: 12.32+/-5.7
 plaque index 0.312
 repaired teeth 65.62%;
 non repaired teeth 12.5%

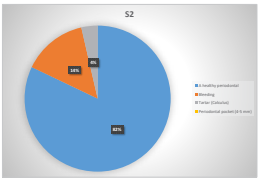
Table 2. Dental status

KEP Index	12.32±5.729		PLAQUE Index				0.3125±0.405	
	S1	S2	S3	S4	S5	S6	S1	S6
A healthy periodontal	42.8%	60.2%	69.8%	58.8%	71.4%	61.7%		
Bleeding	42.8%	16.9%	46.9%	26.7%	28.6%	33.3%		
Tartar (Calculus)	7.1%	6.9%	7.3%	7.1%	6.9%	10.7%		
Periodontal pocket (4-5 mm)	7.1%		7.3%	6.9%				

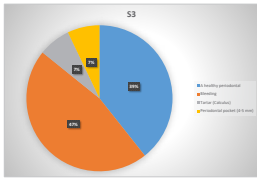
Dental status



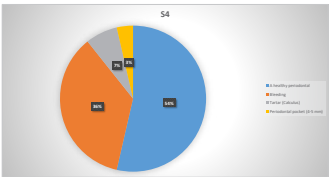
Dental status



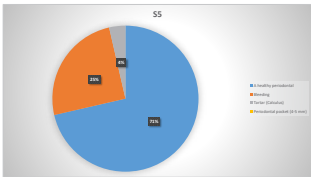
Dental status



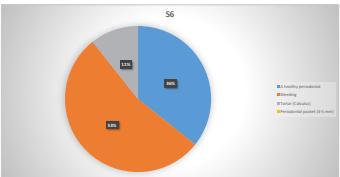
Dental status



Dental status



Dental status



Results of the Second phase

Table 3. Demographic characteristics of the newborns

Values are representing frequency with percentage for gender distribution. Months, Body weight on birth, body weight on the examination are represented with median and interquartile range.

From total number of 40 newborn babies 18 of them were males, and 22 of them were females. When we compare their age in months there isn't any significant difference. Body weight on birth also didn't differ. Body weight on examination was pretty much similar.

Sex	Male N=18 (45%)	Females N=22 (56%)
Months	4,25 (3,50 - 6,0)	4,0 (2,50 - 5,50)
Body weight on birth	3515 (3200 - 3850)	3425 (3170 - 3700)
Body weight on examination	7425 (6580 - 8700)	6730 (6100 - 8170)

There was a significant correlation of LVEDs and mothers eating habits ($\rho = -0.415$, $p = 0.044$), whereby a better value LVEDs determined in infants whose mothers had worse eating habits.

Carotid Intima Media had moderate connection with nutrition intake on both of the carotids, whereby the thicker intima had a pregnant woman with poor eating habits ($\rho = -0.492$, $p = 0.03$).

Table 4. Demographic characteristics of mothers

Mother characteristics					
Age		P1 (22/30)			
	Education		Pregnancy status		
Faculty	22	100%	Normal	30	87.50%
High school	16	40%	With complications	3	7.50%
College	2	4.30%	No data	2	5.00%
Employment status			Alcohol during pregnancy		
Working	30	75%	Yes	1	3.00%
Unemployed	10	25%	No	38	97.00%
Economic status			Cigarette smoking		
Alcohol abuse	3	8%	Yes	0	0%
Average	37	92%	Sometimes	5	12%
			No	35	88%
Other children					
Older and younger child	3	8%			
Younger child	2	4%			
Other child	4	20%			
No other child	27	68%			



IN MOST CASES (58%) MOTHER HAD HIGHER EDUCATION, AND MOST OF THEM DIDN'T HAVE ANY WORKING IN 75% OF CASES.



INCOME WAS AVERAGE IN 82% OF CASES, AND 98% OF THEM DIDN'T HAVE MORE SICKS.



PREGNANCY WAS WITHOUT ANY COMPLICATIONS IN 87.5% CASES.



ONLY 2% OF THEM USED ALCOHOL DURING PREGNANCY, BUT 12% OF THEM SOMETIMES WOULD SMOKE CIGARETTES.

Values are representing frequency with percentage for gender distribution.
Age is represented in median with interquartile range.

Based on eating habits of mothers we have divided subjects in two groups: bad and good eating habits.

Table 5. Eating habits during pregnancy

Food	≥2 daily	Once daily	Several times per week	Once per week	Rarely or never
Milk and dairy products					
Fruit					
Vegetables					
Natural fruit juices					
Non-alcoholic beverage					
Sweets (sugar, candy)					
Sweets (cakes, cookies, chocolate)					
Honey, jam, marmalade					
Candies					
Chips, sticks, snacks					
Meat					
Fish					
Eggs					

Table 6. Eating habits and Echo imaging

Values are shown as median value with interquartile range. p - probability with level of significance set on $p=0.05$

Variable	Bad eating habits	Good eating habits	p
	Median (IQ range)	Median (IQ range)	
DACC	4(3.4-4.7)	4(3.5-4.3)	0.313
LACC	4.1(3.6-4.2)	4.1(3.7-4.2)	0.313
CIMT R	0.04(0.03-0.05)	0.03(0.02-0.04)	0.046*
CIMT L	0.04(0.03-0.04)	0.03(0.03-0.03)	0.015
Am to root	10(5-11)	10(8-10.7)	0.810
MPA	10(5-11.8)	8.5(8-10.5)	0.205
RPA	1.0(1.3-1.6)	2.0(2.3-1.2)	0.411
LPA	2.0(2.3-1.6)	2.0(2.3-1.6)	0.411
RCA	1.4(1.3-1.6)	1.4(1.3-1.2)	0.100
LCA	1.5(1.3-1.7)	1.4(1.3-1.6)	0.037
Ascending aorta	3.7(3-12)	9(8-8.9)	0.024*
CW Doppler flow over AA	2.47(1.48-4)	1.6(1.38-1.88)	0.006
Descending aorta	1.5(1.4-1.5)	1.5(1.5-1.5)	0.014*
CW Doppler Descending aorta	2.3(1.9-3.7)	1.37(1.37-1.67)	0.171
E wave m/s	1.07(0.8-1.26)	1.2(1.1-1.3)	0.115
A wave m/s	0.8(0.75-0.93)	0.84(0.81-0.93)	0.100
Flow over AP	1.3(1-1.4)	1.4(1.3-1.48)	0.014*
RVSD	4(4-4)	4(4-4)	0.372
RVSDd	22(19-26)	19(19-20)	0.001
RVSDv	14(12-15.3)	12(11-13)	0.041*
RVSDv	4.1(3.4-4.4)	4.0(4.1-4.4)	0.140
RVSDv	37(35-39)	38(36-42)	0.409
EPH	69(66-70.5)	69(69-69)	0.083

There is significant difference in carotid intima media thickness in right carotid artery ($p=0,046$).

There was an differences in diameter of descending aorta, with children whose mothers had bad eating habits having larger diameters ($p=0,021$)

Also flow over AP was better in babies from mothers with good eating habits ($p=0,039$)

Left ventricular end diastolic dimension was significantly bigger in newborns from mothers with bad eating habits ($p=0,049$)

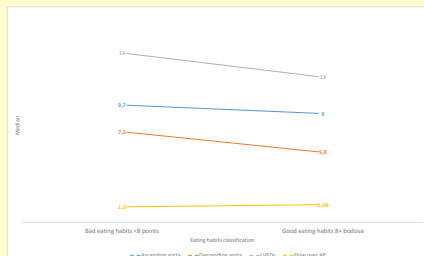


Table 6. EHO characteristics based on KEP index

Variable	KEP <=10	KEP >10	p
	Median (IQ range)	Median (IQ range)	
DACC	4.3 (3.6-4.6)	3.8 (3.6-4.4)	0.441
LACC	4.2 (3.4-4.2)	4.1 (3.3-4.2)	0.641
CIMT R	0.04 (0.03-0.05)	0.035 (0.03-0.045)	0.495
CIMT L	0.035 (0.03-0.04)	0.035 (0.03-0.04)	0.704
The root of aorta	10.5 (10-11)	9.95 (9.50-10.35)	0.181
MPA	10.5 (8.3-11.8)	8.75 (7.15-11.65)	0.295
RPA	3.2 (2-6.2)	2.6 (2.2-4.6)	0.489
LPA	2.9 (2.3-5.5)	2.45 (2.2-3)	0.274
RCA	1.4 (1.2-2)	1.3 (1.1-1.75)	0.402
LCA	1.5 (1.3-1.8)	1.4 (1.2-1.7)	0.710
Ascending aorta	10.5 (9-11.8)	9.05 (9-10.95)	0.706
CW Doppler flow AA	1.85 (1.68-4)	1.78 (1.5-4)	0.388

Descending aorta	79.74(8)	75.8(4.8)	1.000
CW Doppler descending aorta	1.47 (1.04-1)	1.27 (1.37-1)	0.013
E wave m/s	1.15 (1.05-1.2)	1.18 (1.04-1.28)	0.104
A wave m/s	0.76 (0.73-0.84)	0.86 (0.805-0.94)	0.100
Flow over AP	1.38 (1.25-1.4)	1.38 (1.17-1.48)	0.022
RVSD	4.04-4.7	4.05 (4-4.32)	0.196
RVSDd	20 (19-20)	22.05 (18.5-24.5)	0.029
RVSDv	12 (12-16)	14 (13-14.8)	0.001
RVSDv	4.1 (3.5-4.4)	4.4 (3.95-5)	0.022
RVSD	36 (35-37)	38.5 (37-42)	0.004
EPH	68.5 (67-69.5)	68.85 (67-74.42)	0.888

During pregnancy a dental check up has been performed for mothers, KEP index was used as one of the parameters.

Smaller value is better one. Based on that, a value of 10 was used as border one.

Ejection fraction FS% is significantly higher in group of newborns from mothers who had KEP index larger than 10 ($p=0.003$).

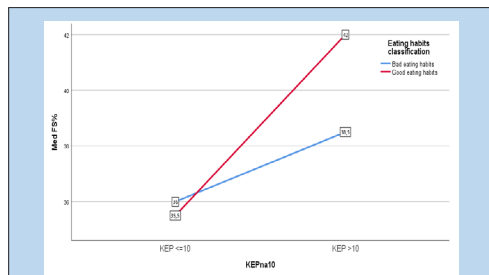
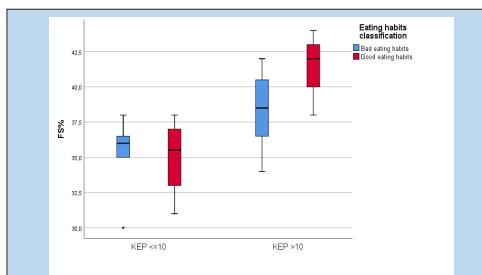


Table 7. The correlation between KEP and Cardiovascular Variables

Correlations		
Variable	Coefficient	KEP index
RCA	rho	-0,693*
	p	0,0047
A wave m/s	rho	,424*
	p	0,044
FS%	rho	,524*
	p	0,01

Only significant correlation are shown

Fortified is a significant correlation between the

- diameter of the right coronary artery and the KEP index,

- where the pregnant woman had better diameters with the **smaller blood KEP Index** ($\rho = -0.693$, $p = 0.047$).

As the KEP rise, the values of RCA were worse.

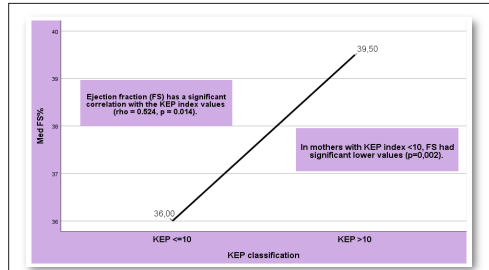


Table 8. The correlation between Parodontosis and Cardiovascular Echo Variables

		Correlation					
Variable	Coefficient	52	53	54	55	56	
Carot1	rho	0.333	0.038	0.478	0.037	0.382	0.407
	p	0.095	0.885	0.052	0.907	0.131	0.025
StA	rho	0.002	0.085	0	0	0.052	0
	p	0.992	0.388	0.928	0.987	0.37	0.714
LA	rho	0.028	0.105	0	0	0.034	0
	p	0.867	0.323	0.42	0.727	0.885	0.848
RCA	rho	0.007	0.153	0.047	0.009	0.716	0.022
	p	0.957	0.158	0.802	0.987	0.005	0.517
LCA	rho	0.008	0.475	0.003	0.002	0.775	0.008
	p	0.957	0.002	0.92	0.987	0.005	0.517
Ascending aorta	rho	0.032	0.793	0.02	0.008	0.233	0.017
	p	0.303	0.14	0.847	0.87	0.203	0.171
CW Doppler flow on AA	rho	0.148	0.204	0.004	0.009	0.301	0.005
	p	0.203	0.121	0.988	0.138	0.018	0.019
Descending aorta	rho	0.189	0.146	0.704	0.146	0.873	0.012
	p	0.178	0.168	0.01	0.187	0.012	0.026
CW Doppler descending aorta	rho	0.186	0.171	0.01	0.011	0.304	0.006
	p	0.178	0.164	0.007	0.007	0.019	0.018
Flow over AP	rho	0.21	0.215	0.006	0.001	0.108	0.007
	p	0.147	0.167	0.002	0.002	0.007	0.007
UTDd	rho	0.008	0.23	0	0	0.03	0
	p	0.911	0.208	0.976	0.976	0.338	0.997
UTDd	rho	0.015	0.204	0.001	0	0.148	0
	p	0.937	0.167	0.988	0.988	0.111	0.988
UTWd	rho	0.011	0.114	0	0.001	0.108	0

Conclusions

The presented cardiovascular-oral health data base for the Balkan region can be used as a geographic, demographic and epidemiologic source of information for the detection and identification of new potential risk factors of individuals for preterm delivery and possible atherosclerosis development.

Primary prevention of atherosclerosis should begin as early as possible, during pregnancy, in childhood, by creating a healthy way of life, which will be able to prevent or at least slow the development of atherosclerosis.

The results so far indicate to the awareness of pregnant women of the importance of oral health and its influence on child development.

However, it is necessary to wait until the end of the study to see definitive results, the impact of mothers oral health on the developing fetus.

There was a significant connection between diet and oral health status of mothers with some segments of the development of cardiovascular system in infants.

It is necessary to extend the study and test inference on a larger sample.

Final results of the research

Regular dental therapy can decrease the frequency of the appearance of caries, periodontal disease in pregnant women, the frequency of prematurity, low birth weight (with all its potential complications, decrease the financial costs of neonatal intensive care management and cardiovascular repercussions on a newborn's health.

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THE IMPACT OF ORAL HEALTH AND DIETARY HABITS OF THE PREGNANT WOMAN ON THE DEVELOPMENT OF FETAL AND NEWBORNS CARDIOVASCULAR SYSTEM

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Abstract

Objectives: The aim of the study was to evaluate the relationship between the oral health of mothers, dietary habits during pregnancy with the development of the fetal vascular system, specifically coronary and carotid arteries. **Methods:** It was designed as a cohort study, including pregnant women selected by random selection from a total number of pregnant women examined in private clinics in Mostar, Sarajevo, and Komiža (Croatia). To implement the principles of ethical and bioethical research, approval of the ethics committee was obtained. All selected patients had signed an informed consent form. **Results:** Newborns from mothers with bad eating habits had significantly higher values of the right carotid artery intima-media thickness ($p=0.046$). There was a statistically significant difference in the diameter of the descending aorta, with larger diameters in children whose mothers had bad eating habits ($p=0.021$). Flow rate over pulmonary artery was higher in babies from mothers with fiber-rich, lower-fat eating habits ($p=0.039$). Oral health was examined with the Decay-missing-filled index (DMF). Ejection fraction (FS%) was significantly higher in the group of newborns whose mothers had a larger DMF index ($p=0.03$). **Conclusion:** The authors found

that dietary habits and oral health of pregnant women have a significantly affect the diameter of blood vessels and flow rate.

Key words: Atherosclerosis, Intima-Media Thickness, DMF index, Dietary habits, Ejection fraction

Introduction:

Oral health and eating habits during pregnancy have the potential to affect pregnancy outcomes. Some observational studies have indicated a significant association of periodontal disease with adverse pregnancy outcomes, but others have not [1, 2]. Bad oral health during pregnancy, due to the higher concentrations of estrogen and progesterone can induce hyperemia, edema, and bleeding in periodontal tissues [3]. In 1996, Offenbacher and colleagues [4] first reported a potential association between maternal periodontal disease and delivery of a preterm/low birth weight infant. In a case-control study of 124 pregnant women, they observed that women who delivered before 37th gestation week or infants weighing <2500 g had significantly worse periodontal disease than women in the control group.

The incidence of periodontal disease is correlated with bad eating habits through life, with pregnancy only speeding up the process. U.S. Department of Agriculture have wrote; in one of their guidelines: “Healthy eating during pregnancy is critical to a fetal growth and development” [5]. Gale R.C. et al. in their study have noted that some autopsy studies show that intimal lipid accumulations in arteries are often present at birth, suggesting that the prenatal environment plays a role in the pathogenesis of atherosclerosis [6]. In animal models, a restricted or unbalanced maternal diet during gestation can influence susceptibility to atherosclerosis, but the relationship in humans between maternal diet during pregnancy and atherogenesis is unknown [6]. The main source of vitamins and nutrients needed during pregnancy should come from diet, but daily prenatal vitamins can slightly help fill gaps. Prenatal vitamins are one of the reasons that even with bad eating habits and poor oral hygiene, most of the pregnancies end with a good outcome – a healthy new-born. The impact of mother’s nutrition and their oral health on cardiovascular fetal system development, can lead to a slower fetal development, lower birth weight, as well as differences in blood vessel development [7].

It is presently known that atherosclerosis begins in childhood and continues for a long time without manifesting symptoms, it is increasing with age until it begins to affect health. Maternal transmission of risk for atherosclerosis is proven [8] and recent experiments in genetically more homogeneous

rabbits established that temporary diet-induced maternal hypercholesterolemia is sufficient to enhance fetal lesion formation [9]. Based on that, even atherosclerosis could have its roots in the fetal period, but that is still unconfirmed. Generally, pregnant women with chronic periodontitis are more likely to have preterm birth and/or newborns with small birth weight.

This study aimed to evaluate the relationship between the oral health, dietary habits during pregnancy and the development of the fetal vascular system, specifically coronary and carotid arteries. The second aim was to assess the connection of dietary habits and maternal oral health with gestation age.

Patients and methods:

“Cardiovascular Disease and Oral Health - The impact of pregnant women’s oral health on the cardiovascular health of children” is a project that is run by the Committee of the Cardiovascular Disease Department of Medical Sciences ASA of Bosnia and Herzegovina. It has started in 2017, with the first phase of research being completed according to plan in 12 months. The second phase lasted for two years (2017-2019). It was designed as a cohort study, including pregnant women selected by random selection from a total number of pregnant women examined in private clinics in Mostar, Sarajevo, and Komiža (Croatia). Randomization was done using Microsoft Excel software, in the database with all patients who were examined or had a scheduled examination at the Clinic. To implement the principles of ethical and bioethical research approval of the ethics committee was obtained. All selected patients had signed an informed consent form.

In the first phase of the study, 43 pregnant women from Mostar and Sarajevo in Bosnia and Herzegovina and from Komiža in Croatia were included. All mothers from Komiža went to the Split Clinical Hospital Center for routine examinations. During pregnancy, general health was examined, as well as life habits and oral health habits using standardized questionnaire, and anthropometric and blood pressure measurements were taken. Researchers have made two questionnaires for mothers: the first one about their dietary plan and the second one about oral hygiene practice and their oral hygiene knowledge. Eating habits were analyzed based on the guidelines of the World Health Organization [10], and optimal eating habits were graded with 1, vice versa bad eating habits with 0. Also, a standardized check-up list for dentists was made. Dentists examined their oral cavity, and the condition was described with Decayed, Missing, Filled (DMF) index, Plaque index and

periodontal disease presence [11]. After giving birth, 40 mothers and newborns continued, their follow-up, with only three lost participants, who left the study on their own. In the second phase of the study, echocardiography was performed, when children's were 6 months old; including Color and CW /Continuous wave/ Doppler measuring. In all children, we imaged regions of interest using a high-resolution ultrasound Color CW Doppler machine with automated Intima-Media Thickness measurement software. Standard echocardiography for newborns and infants according to criteria of the "Association for European Pediatric and Congenital Cardiology (AEPC) was done in Sarajevo, Mostar and Split [12]. All mentioned centers had an ultrasound machine for pediatric echocardiography with pediatric transducers. We have used:

- Transthoracic echocardiography /TTE/ during examination;
- Transducers for echocardiography: 5 MHz and 2.5 MHz
- Techniques of examination: M, B mode, Doppler /PW- pulse wave and CW-Continuous wave/, Color Doppler echocardiography
- Views: subcostal 4CH view, subcostal RVOT/right ventricular tract out-flow/, vena cava inferior and abdominal aorta
- Parasternal long and short axis, LV short axis: level of mitral valve and papillary muscles
- Suprasternal long and short axis view.

Machines that were used are; Toshiba Adlio 300 in Sarajevo, Siemens Acuson S1000 in Mostar and Vivid S70N in Split.

Echocardiography has been performed by pediatric cardiology subspecialists, in total 4 of them in Bosnia and Herzegovina and in Croatia. They have analyzed morpho-haemodynamics including diameters, ejection fraction and flow through the vessels. Others researchers were gynecologists, general pediatricians, nutritionists, dentists, radiologists and epidemiologists.

Statistical analysis:

The statistical analysis was performed using SPSS software (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp). The normality of distribution was analyzed by a Shapiro-Wilk test. The statistical differences between the two groups were analyzed by Mann Whitney U test. Median and interquartile range values were presented. The correlations between DMF index, eating habits and color Doppler findings were analyzed using Spearman's rho correlation coefficient. Results were considered significant at the level of $p < 0.05$.

Results

In our study, average age of pregnant women was 25 years, ranging from 20 to 32 years. : From a total number of 40 pregnancies, 36 (90.3%) went without any complication. There were 28 (71%) of women with a university-level education, whereas others had a high school diploma. During pregnancy, 2 participants (5%) experienced some severe disease. Questionnaire on mothers' eating habits showed that 19 out of 40 (48.4%) participants consumed dairy products daily, 26 out of 40 (65%) participants consumed fruits at least twice per day; furthermore 9 out of 40 (22.6%) participants consumed vegetables at least twice per day. The 17 out of 40 (42.5%) participants consumed meat daily, also 18 of 40 (45%) participants consumed meat a few times during a week. Once per week fish meal was consumed by 13 of 40 (33.3%) participants, and 14 of 40 (35.8%) participants did not consume fish at all. Alcohol was consumed by 1 (2.5%) participant, and cigarettes by 2 (5%) participants. Oral hygiene knowledge and practice questionnaire showed that 27 (67.5%) participants thought they should brush their teeth at least twice daily and 13 (32.5%) after every meal. Similar results are in practice, with 32 of 40 (80%) participants brushing their teeth in the morning and evening, 3 of 40 (7.5%) just in the evening and 1 (2.5%) just in the morning. The 22 out of 40 (55%) visited the dentist twice last year, and most often, the cause was a regular check-up. The 14 out of 40 (35%) participants reported that tooth repair was the cause for visiting dentists. The average Decay-missing-filled index (DMF) index had median of 10.50 with interquartile range of 5 to 15.5. From the total number of participants, 26 (65.6%) had repaired teeth and only 5 (12.5%) participants had all healthy teeth. In the second phase, we have analyzed the newborns. The demographic characteristics and bodyweight of the newborns are shown in table 1.

Table 1. Demographic characteristics of the newborns

Sex	Male N=18 (45%)	Females N=22 (55%)	Mann-Whitney	p
Childs' age at examination median (min-max age in months)	4,25 (2 - 14)	4,0 (1,0-12,0))	162,500	0.332
Newborn's weight (grams) median (IQ range)	3515 (3200 - 3850)	3425 (3170 - 3700)	159.500	0.295
Weight at examination (grams) median (IQ range)	7425 (6580 - 8700)	6730 (6100 - 8170)	158.500	0.282

Based on the eating habits of mothers we have divided participants into two groups: 16 out of 40 (40%) had bad eating habits and 24 out of 40 participants

had optimal eating habits according to WHO. Color Doppler findings in their children are shown in table 2.

Table 2. Eating habits and Echo imaging

Variable	Unit	Poor eating habits	Optimal eating habits	Mann Whitney	p
Right common carotid artery diameter	mm	4(3.8-4.7)	4(3.5-4.35)	19.50	0.323
Left common carotid artery diameter	mm	4.1(0.03-4.2)	4.1(3.7-4.2)	26.00	0.811
Right carotid artery intima-media thickness	mm	0.04(0.03-0.05)	0.03(0.02-0.04)	16.00	0.046*
Left carotid artery intima-media thickness	mm	0.04(0.03-0.04)	0.03(0.03-0.03)	15.50	0.053
Aortic root diameter	mm	10(9.5-11)	10(8.8-10.7)	63.50	0.810
Main Pulmonary artery diameter	mm	10(8.2-11.8)	8.5(8-10.5)	50.00	0.296
Right Pulmonary artery diameter	mm	3.2(2.2-5.8)	2.6(2.3-3.2)	50.00	0.411
Left Pulmonary artery diameter	mm	2.8(2.3-5.1)	2.8(2.3-2.9)	46.00	0.402
Right coronary artery diameter	mm	1.4(1.2-1.9)	1.4(1.1-2)	56.50	0.509
Left coronary artery diameter	mm	1.5(1.3-1.7)	1.4(1.2-1.6)	54.00	0.417
Ascending aorta (AA) diameter	mm	9.7(9-12)	9(8.8-9)	31.50	0.029*
CW Doppler flow over AA	m/sec	2.48(1.68-4)	1.62(1.38-1.88)	29.50	0.300
Descending aorta (DA) diameter	mm	7.5(5.8-8.5)	5.8(5-7)	29.00	0.021*
CW Doppler flow over DA	m/sec	2.34 (1.55-7)	1.58 (1.37-1.67)	25.50	0.171
E wave m/s	m/sec	1.07(0.9-1.29)	1.2(1.13-1.3)	47.50	0.233
A wave m/s	m/sec	0.82(0.75-0.95)	0.84(0.81-0.93)	57.50	0.550
Flow over pulmonary artery	m/sec	1.3(1-1.4)	1.48(1.4-1.48)	33.00	0.039*
IVSd	mm	4(4-4.4)	4(4-4.3)	53.50	0.371
LVEDd	mm	22(19-25)	19(18-20)	39.50	0.091
LVEDs	mm	14(12-15.3)	12(11-13)	35.50	0.049*
LVPWd	mm	4.1(3.4-4.6)	4.6(4.1-4.6)	43.50	0.149
FS%	%	37(35-39)	38(36-42)	56.00	0.489

CW Doppler - continuous wave Doppler; AA – Ascending aorta; DA- Descending aorta; IVSd - indicates septal wall thickness at end diastole; LVEDd - indicates Left Ventricle end diastolic dimension; LVEDs – indicated Left Ventricle end systolic dimension; LVPWd - indicates posterior wall thickness at end diastole; FS% - Fractional shortening (%)

Newborns from mothers with bad eating habits had significantly higher values of the right carotid artery intima-media thickness ($p=0.046$). There was a statistically significant difference in the diameter of descending aorta, with larger diameters in infants whose mothers had bad eating habits ($p=0.021$). Flow over AP was higher in infants from mothers with optimal eating habits ($p=0.039$).

The positive correlation was found between LVEDs and mothers bad eating habits ($r=0.415$, $p=0.044$). Carotid intima-media thickness had a positive correlation with nutrition intake on both of the carotids, whereby the thicker intima was in infants whose mothers had poor eating habits ($r=-0.492$; $p=0.03$).

As an indicator for mothers, dentists used the DMF index. DMF index with smaller values showed better oral health, and a value of 10 is used as a cut off value between adequate and insufficient oral health quality.

We compared the values of analyzed Color Doppler findings in children and in most cases, there was not any difference (Table 3).

Table 3. Mothers DMF index and newborns Color Doppler findings

Variable	Unit	DMF ≤ 10	DMF > 10	Mann Whitney	p
Right common carotid artery diameter	mm	4.3 (3.6-4.6)	3.8 (3.6-4.4)	18.50	0.441
Left common carotid artery diameter	mm	4.2 (3.4-4.2)	4.1 (3.3-4.2)	21.00	0.641
Right carotid artery intima-media thickness	mm	0.04 (0.03-0.05)	0.035 (0.03-0.045)	32.50	0.495
Left carotid artery intima-media thickness	mm	0.035 (0.03-0.04)	0.035 (0.03-0.04)	36.00	0.704
Aortic root diameter	mm	10.5 (10-11)	9.95 (8.9-10.35)	44.50	0.181
Main Pulmonary artery diameter	mm	10.5 (8.3-11.8)	8.75 (7.65-11.65)	49.00	0.295
Right Pulmonary artery diameter	mm	3.2 (2-6.2)	2.6 (2.2-4.6)	50.00	0.489
Left Pulmonary artery diameter	mm	2.9 (2.3-5.5)	2.45 (2.2-3)	39.50	0.274
Right coronary artery diameter	mm	1.4 (1.2-2)	1.3 (1.1-1.75)	52.50	0.402
Left coronary artery diameter	mm	1.5 (1.3-1.8)	1.4 (1.2-1.7)	60.00	0.710
Ascending aorta (AA) diameter	mm	10.5 (9-11.8)	9.05 (9-10.95)	60.00	0.706
CW Doppler flow over AA	m/sec	1.85 (1.68-4)	1.78 (1.5-4)	34.50	0.388
Descending aorta (DA) diameter	mm	7 (5,7-8.5)	7.5 (5.6-8.2)	66.00	0.989
CW Doppler flow over DA	m/sec	1.67 (1.58-5)	1.57 (1.37-7)	35.00	0.412
E wave m/s	m/sec	1.15 (1.05-1.3)	1.16 (0.9-1.28)	56.50	0.558
A wave m/s	m/sec	0.76 (0.73-0.84)	0.885 (0.815-0.94)	41.50	0.130
Flow over pulmonary artery	m/sec	1.38 (1.15-1.4)	1.39 (1.17-1.49)	53.00	0.422
IVSd	mm	4 (4-4.7)	4.05 (4-4.35)	53.00	0.395
LVEDd	mm	20 (19-22)	22.65 (18.5-24.5)	58.00	0.620
LVEDs	mm	13 (12-14)	14 (11-14.8)	65.00	0.951
LVPWd	mm	4.1 (3.5-4.6)	4.4 (3.95-5)	47.50	0.252
FS%	%	36 (35-37)	39.5 (37.5-42)	18.00	0.003

CW Doppler - continuous wave Doppler; AA – Ascending aorta; DA- Descending aorta; IVSd - indicates septal wall thickness at end diastole; LVEDd - indicates Left Ventricle end diastolic

dimension; LVEDs – indicated Left Ventricle end systolic dimension; LVPWd - indicates posterior wall thickness at end diastole; FS% - Fractional shortening (%)

Mothers' bad eating habits negatively correlated with the diameter of children's descending aorta ($r=-0.508$, $p=0.011$), meaning the more the bad habits were present the smaller were the children's diameters of descending aortas.

REVIEWER: Mothers' bad eating habits negatively correlate

ANSWER: Before this sentence in earlier version was Figure 1, which was removed after receiving last review of our paper. So sentence before, isn't connected with the DMF, instead with choice of food (optimal vs poor).

Furthermore, parodontal disease were directly correlated with diameters of left and right pulmonary artery, especially segments S3 and S4, which have also been correlated with Flow rate over AP (table 4).

Table 4. Correlation between periodontal disease and Color Doppler findings

Variable	Coefficient	Segment					
		1	2	3	4	5	6
Left carotid artery intima-media thickness	Rho	0.331	0.038	0.478	.629	0.382	.540
	P	0.195	0.885	0.052	0.007	0.131	0.025
Right pulmonary artery diameter	Rho	.496	0.389	.728	.749	.537	.774
	P	0.022	0.081	0	0	0.012	0
Left pulmonary artery diameter	Rho	.490	0.323	.747	.772	.475	.761
	P	0.028	0.165	0	0	0.034	0
Right coronary artery diameter	Rho	.560	0.151	.543	.572	0.065	.484
	P	0.007	0.502	0.009	0.005	0.774	0.022
Left coronary artery diameter	Rho	.552	0.159	.605	.629	0.065	.551
	P	0.008	0.479	0.003	0.002	0.775	0.008
Ascending aorta diameter	Rho	.458	0.062	.492	.548	0.265	.504
	P	0.032	0.783	0.02	0.008	0.233	0.017
CW Doppler flow on AA	Rho	0.355	0.314	.646	.593	0.258	.711
	P	0.148	0.204	0.004	0.009	0.301	0.001
Descending aorta diameter	Rho	-0.201	-0.321	-0.068	0.136	-0.036	0.019
	P	0.369	0.146	0.764	0.546	0.873	0.932
CW Doppler descending aorta	Rho	0.276	0.164	.587	.583	0.242	.620
	P	0.268	0.517	0.01	0.011	0.334	0.006

Variable	Coefficient	Segment					
		1	2	3	4	5	6
Flow over pulmonary artery	Rho	-0.278	-0.264	-.565	-.556	-0.219	-.558
	P	0.21	0.235	0.006	0,007	0.328	0.007
LVEDd	Rho	.542	0.267	.712	.723	.456	.709
	P	0.009	0.23	0	0	0.033	0
LVEDs	Rho	.511	0.208	.676	.718	0.338	.693
	P	0,015	0,354	0,001	0	0,124	0
LVPWd	Rho	-.531	-0.347	-.698	-.664	-0.311	-.698
	P	0.011	0.114	0	0.001	0.159	0

Values represent Spearman's rho coefficient, p – probability, level of significance is set on $p < 0.05$
 CW Doppler - continuous wave Doppler; AA – Ascending aorta; DA- Descending aorta; LVEDd - indicates Left Ventricle end diastolic dimension; LVEDs – indicated Left Ventricle end systolic dimension; LVPWd - indicates posterior wall thickness at end diastole;

DISCUSSION

Although this study started with the idea to assess the impact of oral health and nutrition on the incidence of preterm birth and low birth weight, results of this study have shown the existence of a connection with fetal vascular system development.

Based on dietary habits, in the right carotid artery, a significant difference was found in intima-media thickness ($p=0.046$). There was a statistically significant difference in the diameter of descending aorta. Flow over AP was higher in infants from mothers with optimal eating habits ($p=0.039$).

In the study conducted by Hugh Silk, Alan Douglass etc. [13] it is mentioned that only 22 to 34% of woman in the USA consult a dentist during pregnancy. Even when an oral problem occurs, only one half of pregnant women tend to visit a dentist.

Mostly periodontitis is reason to visit dentist. Periodontitis has been observed with several poor pregnancy outcomes [13,14]. In our study, authors showed the difference in some parameters between two groups of participants divided according to their eating habits. In a systematic review of mainly cross-sectional, case-control, and cohort studies conducted between 1996 and 2006 in 12 countries and three states, investigators identified 24 studies demonstrating a positive relationship between periodontitis and preterm birth, low birth weight, or both [14]. These studies involved approximately 15,000 mothers. Three of the studies were randomized controlled trials

(RCTs). Conversely, 14 studies reported no relationship between periodontitis and poor pregnancy outcomes. A recent, large, U.S.-based RCT found no connection between periodontitis and preterm birth and low birth weight [15].

Using DMFT index, we have conducted that mothers who had bad eating habits also had increased values of DMFT index. Ananda Dasanyake in her study [16] used DMFT index and showed that mothers with bad oral hygiene had higher values of DMFT index. In addition, their children had OR=1.1. (0.9 to 1.4) for Low birth weight. In our study did not have children with low birth weight. Preterm birth, delivery at less than 37 weeks' gestation, occurs in approximately 12% of all births [17]. In our study all babies were delivered at least in 37th week. Jeffcoat et al. [18] examined the relationship between maternal periodontal disease and spontaneous preterm birth among 1313 pregnant women and found that moderate/severe maternal periodontal disease identified early in pregnancy was observed in the group of spontaneous preterm birth, independent of other traditional risk factors.

Moore et al. [19] in a follow-up longitudinal study of 3738 women found no association between maternal periodontal disease and preterm birth. However, there was an increase in second trimester fetal loss rate among women with periodontal disease.

Eating habits showed direct impact on fetal vascular growth and specifically on intima-media thickening. Thompson J.M. et al. [20] in their study showed the association between dietary patterns in pregnancy and small for gestational age (SGA) infants. In logistic regression models of SGA, at a univariate level, traditional diet scores (low-fat, oat-rich, fresh food, including fish and Mediterranean cuisine) in early pregnancy showed a protective effect for an SGA infant (OR ¼ 0.79; 95% CI 0.70, 0.89), while in late pregnancy, the effect was similar (OR ¼ 0.83; 95% CI 0.74, 0.94). When both time periods were put in a model together, the effect of diet in early pregnancy remained significantly associated with SGA and that of late pregnancy was no longer significant. The junk and fusion diet scores showed no significant effect on SGA. His conclusion was that maternal diet, particularly in early pregnancy, is important for the development of fetus. Sociodemographic factors tend to be significantly related to dietary pattern, suggesting that extra resources may be necessary for disadvantaged mothers in order to be able to purchase more healthy foods, which tend to be more expensive than high-energy foods. Authors are of the opinion that, good eating habits during pregnancy are essential for the future health of the unborn child.

Maternal diet during pregnancy and its impact on carotid intima-media thickness in children was examined by Gale C. et al [6]. Increased Intima Media Thickness (IMT) was associated with a lower maternal energy intake in early ($p=0.029$) or late ($p=0.006$) pregnancy, after adjustment for these factors. Intima Media Thickness was greater in children whose mothers had lower energy, protein, fat, and carbohydrate intake in either early or late pregnancy. Akbari-Sedigh A et al. have assessed [21] dietary intake using a valid and reliable food frequency questionnaire and dietary patterns were derived by factor analysis. Measurement of cIMT was performed by means of ultrasonography for the wall of common carotid artery. In comparison with our study that had two dietary patterns, three dietary patterns were identified in their study, which accounted for 23.0% of the total variance, including the healthy, the traditional, and the unhealthy patterns. After adjusting for age, sex, pubertal status, smoking exposure, physical activity, body fat percentage, and intake of magnesium and energy, a significant inverse association was observed between the healthy dietary pattern and cIMT ($\beta=-0.131$, $p=0.019$), whereas none were found between cIMT and the traditional ($\beta=-0.004$, $P=0.932$) and the unhealthy dietary ($\beta=0.004$, $P=0.942$) patterns. Results of their study indicate that adherence to healthy dietary pattern could prevent increased cIMT in children and adolescents with overweight and obesity. Contrary to Akbari Sedighs findings, in Da Silva's study [22] there was a significant correlation between unhealthy dietary pattern and cIMT. In our study unhealthy eating habits were significantly correlated with cIMT, with cIMT of right carotid artery being significantly thicker in group with unhealthy eating habits.

Limitations of the study

Major limitation of this study was a small number of patients per center. Also, eating habits were classified based on the questionnaire. Autoimmune illnesses or long drug intake wasn't analyzed profoundly. Economic status was not taken in consideration either.

CONCLUSION

Based on the results, in our study we found that bad eating habits had an impact on the diameter of blood vessels and on flow. Unhealthy dietary plans will most probably lead to bad oral health and presence of periodontitis, which could contribute to the thickening of carotid intima-media. Finally,

that mechanism could contribute to the development of atherosclerosis. Due to the small sample in this study, and for better confirmation, it is necessary to extend the study and test inference on a larger sample.

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ARCHIVES OF DISEASE IN CHILDHOOD

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Highlights from this issue:

Morphine or hydromorphone: which should be preferred?
Evolving management of paediatric portal hypertension
Perinatal outcomes among births to women with infection during pregnancy
Improved quality of reporting safety data of medication in paediatric randomised controlled trials
Cystic fibrosis transmembrane conductance regulator modulators for cystic fibrosis: a new dawn?

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physical health of children all while describing the various ways that one can work with children along with some of the challenges that the experts face each day along with some of the children's experiences.

23 PEDIATRICIAN AND EDUCATIONAL REHABILITATOR – ASSOCIATES IN THE PROCESS OF OBSERVATION, DIAGNOSIS AND REHABILITATION OF CHILDREN WITH DEVELOPMENTAL DISABILITIES

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The number of children with disabilities and persons with disabilities is continuously increasing, which is evident from the data of the Croatian Institute of Public Health. The report on persons with disabilities in the Republic of Croatia, May 2019, lists 45,314 children with disabilities. The pediatrician, as a doctor who deals with the health care of children from birth to the end of adolescence and cares about improving the child's health and eliminating risk factors that threaten his normal growth and development, certainly has children with disabilities and developmental difficulties among his patients. An important part of any systematic examination of a child should be an assessment of psychomotor development and monitoring developmental milestones. When it comes to children with disabilities it can also include information obtained from co-specialists. The competencies of pediatricians include the promptly detection of developmental delays, knowledge of various developmental disabilities, and also perspective of related co-experts within different systems.

In providing support to children with disabilities, educational rehabilitators are important part of the interdisciplinary diagnostic team, the team of early intervention experts and professional teams in kindergartens and schools. They are a profession whose diagnostic, educational and rehabilitation procedures and programs apply to children with disabilities and persons with disabilities, the population with visual impairment, learning difficulties, attention deficit hyperactivity disorder, motor disorders, chronic diseases and multiple disabilities. The actions of both, the pediatrician and the educational rehabilitator, are aimed at the well-being of the child with risk factors, developmental delays or identified developmental difficulties. Mutual cooperation should include the exchange of key information and trust in the assessment, competencies and recommendations.

It is particularly important in case of children with autism spectrum disorder, which is primarily characterized by difficulties in social communication and interaction and limited, repetitive patterns of behavior, interests, and activities. During the periodic systematic examination in the pediatric clinic, the mere presence of the parents and the learned strategies can mask the characteristic difficulties. In some children, symptoms are present at an early stage of development, but often become more apparent when social demands exceed the child's current abilities. They are more pronounced during the child's time in kindergarten or school, which is then noticed by other professional associates – educational rehabilitator.

If the parent is not concerned about the child's development, finds it difficult to accept the possibility of the difficulty

or denies it, sometimes is missing the transfer of key informations in sequence „educational rehabilitator – parent – pediatrician“, which unfortunately slows down the process of diagnosis and intervention. As an example of good practice and cooperation between a pediatrician and an educational rehabilitator for the purpose of objective informing, we provide and recommend a written opinion about the developmental status of the child.

24 PRESENCE OF LANGUAGE DISORDERS IN SCHOOL AGE

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Language difficulties refer to impaired language acquisition and impaired language processing and can be an integral part or one of multiple difficulties. The most common among them is developmental language disorder, which refers to the present difficulties in the domain of language. Developmental language disorder is diagnosed when a child, despite orderly general cognitive abilities and a stimulating environment, has difficulty learning his mother tongue, and then any other language.

The paper presents the results of the analysis of the presence of developmental speech disorder in users of psychosocial support services in the Zagreb County. Linguistic comprehension was examined and the obtained results were analyzed by a qualitative methodology.

We emphasize the awareness of parents, professionals and all those involved in the upbringing and education of the child as a prerequisite for partnership with students and providing the necessary support to students in working with difficulties in the field of language comprehension.

General Pediatrics

25 CHILD'S BLOOD VESSEL DEVELOPMENT IN RELATION TO MOTHER'S DIETARY EATING HABITS AND ORAL HEALTH

Senka Meshovic Dinarevic*, Anes Jogunčić, Kristen Sarić, Lutovo Šporišević, Berislav Topić, Vjekoslav Krželj, Liana Cambj-Sapunar, Davor Petrović, Sanja Jurišić, Senad Sarić, Samir Prohić. Polyclinic Eurofarm

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Dietary eating habits and oral health of pregnant women have the potential to affect pregnancy outcomes. Some observational studies have indicated a significant association of the periodontal disease with adverse pregnancy outcomes, such as the risk of preterm delivery and differences in blood vessels development.

The aim of the study was to evaluate the relationship between the dietary eating habits of mothers and their oral health during pregnancy with the development of the coronary and carotid arteries including intima media thickness.

By random selection, 40 pregnant women and their newborns formed a cohort – pilot study. The approval of the ethics committee was obtained. During pregnancy eating habits and dental mother's status were analyzed. After delivery, a

Abstracts

detailed color Doppler echocardiography including carotid vessels has been performed. Newborns from mothers with bad eating habits had significantly higher values of the right carotid artery intima-media thickness/CAIMT/ $(p=0.046)$. Oral health was examined with DMF index/Decayed, Missing, Filled/. A significant correlation between the diameter of the right coronary artery and the DMF index was proven, where the pregnant woman had better diameters with the smaller DMF Index ($\rho = -0.693$, $p = 0.047$). CAIMT had a moderate connection with nutrition intake on both of the carotids, whereby the thicker intima had a pregnant woman with poor eating habits ($\rho = -0.492$, $p = 0.03$). There was a statistically significant difference in the diameter of descending aorta, with larger diameters in children whose mothers had bad eating habits ($p=0.021$). Flow over AP was better in newborns from mothers with good eating habits ($p=0.039$). Fraction shortening/FS% was significantly higher in newborns whose mothers had a larger DMF index ($p=0.03$). There was a significant correlation of LVEDs/left ventricle end-diastolic diameter/and mothers eating habits ($\rho = -0.415$, $p = 0.044$), whereby a higher value LVEDs determined in infants whose mothers had worse eating habits. Dietary eating habits and oral health of pregnant women have a significant connection with some segments of cardiovascular system development. Eating habits have an impact on the diameter of blood vessels and on flow.

Unhealthy dietary plans will most probably lead to bad oral health and the presence of periodontitis, which could contribute to the CAIMT and the development of atherosclerosis. It is necessary to extend the study and test inference on a larger sample.

26 FAMILIAL HYPERCHOLESTEROLEMIA: A RARE CASE OF EARLY DIAGNOSIS

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Familial hypercholesterolemia (FH) is a common life-threatening genetic condition that causes high cholesterol and leads to a much higher-than-normal risk of coronary heart disease (CHD). The heterozygous type is found in about 1 out of 300-500 people, the homozygous type is quite rare in 1 out of 1 million people.

Objective To analyze the clinical case of family hypercholesterolemia in sibs.

Patients and Methods In 3 siblings (from triplets) at the age of 7 years randomly detected new-onset hypercholesterolemia 5.97 mmol/L, 5.65 mmol/L, 6.43 mmol/L. In a second study after 14 days, hypercholesterolemia persists (6.11 mmol/L, 5.67 mmol/L and 6.49 mmol/L, respectively). Two siblings (identical) had high cholesterol levels (4.060 mmol/L and 4.413 mmol/L) due to low density lipoprotein (LDL). The third child with the lowest level of hypercholesterolemia had normal LDL and a high level of high density lipoprotein (HDL). No evidence of secondary hypercholesterolemia (diabetes mellitus, chronic renal insufficiency, hypothyroidism, cholestatic hepatitis, iatrogenic illness) was found.

A mother (42 years old), sticks to a strict diet with a reduced fat content, but hypercholesterolemia persists, statins

therapy is not conducted, recommendations for examining children have not been received.

Results Plasma LDL cholesterol level of 4.0 mmol/L or higher in follow-up blood test, provided parents with hypercholesterolemia, confirms the FH in two children from triplets.

At the same time, there are no external physical signs of the disease in children (xanthomas, corneal arch, xanthelasma). This, along with relatively low hypercholesterolemia, suggests a prognostically favorable Heterozygous Familial Hypercholesterolemia. Genetic screening for the presence of FH is not required to confirm the diagnosis, but may be useful if the diagnosis is ambiguous.

A strict diet with a reduced fat content was recommended to patients, as well as supervision of a cardiologist and lipid screening. It was decided that at the age of 8-10 years, while maintaining LDL cholesterol >4.0 mmol/L in follow-up blood test would be observed even on the recommended diet, the treatment with low doses of statins would be discussed.

Conclusion Despite the prevalence of FH and the availability of effective treatment, FH is rarely diagnosed in children. This emphasizes the importance of lipid screening in childhood and cascading screening of all members of the patient's family for the prevention of CHD.

27 ANTHROPOMETRIC DIMENSIONS OF THE ARAL SEE REGION (KARAKALPAKSTAN, REPUBLIC OF UZBEKISTAN) NATIVES MAY REFLECT NEGATIVE INFLUENCE OF PESTICIDE ENDOCRINE DISRUPTOR CHEMICALS ON THE POSTNATAL ONTOGENESIS

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The aim of the study was revelation of the specific tendencies of the physique development in subjects born and grown up at various distances from the former Aral Lake disaster (ALD) as a possible factor determining exposure window of organochlorine pesticides (OCPs) during the body growth. ALD was a combined result of essential climate aridization and anthropogenic pollution with the excessive application of OCPs in a droughty agricultural region.

A complex anthropometric study including measurement of body mass and length, the size of extremities, pelvis and of skinfold thickness was carried out on 310 volunteers of both sexes. All of them had been born in 1990 – 1995 before the start of effective measures for liquidation of the ALD consequences. The volunteers were divided into three groups, attached to geographical zones: first – zone of ALD, northern part of the region around the town of Muynak; second zone, relatively safe – central part, around the city of Nukus; third zone, safe – the southern part of the region.

The comparison of anthropometric parameters was statistically measured using Kruskal-Wallis test and Mann-Whitney criterion including Bonferroni correction for multiple comparison.

Males from the first group possessed statistically valuable lower body mass, arm length, size of the chest and major joints, waist perimeter, skinfold thickness in comparison to subjects from other groups. In contrast, females from the

Child's blood vessel development in relation to mother's dietary eating habits and oral health

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Vjekoslav Krželj⁶, Liana Cambj-Sapunar⁷, Davor Petrović⁸, Sanja Jurišić⁹, Senad Sarić¹⁰, Samir Prohić¹¹

Introduction

- Dietary eating habits and oral health of pregnant women have the potential to affect pregnancy outcomes. Some observational studies have indicated a significant association of periodontal disease with adverse pregnancy outcomes, such as risk of preterm delivery and differences in blood vessels development.

Methods & Objectives

The aim of the study was evaluate the relationship between the dietary eating habits of mothers and their oral health during pregnancy with the development of the coronary and carotid arteries including intima media thickness.

Patients and methods:

By random selection, 40 pregnant women and their newborns formed a cohort - pilot study. The approval of the ethics committee was obtained. During pregnancy eating habits and dental mother's status were analysed. After delivery a detailed colour Doppler echocardiography including carotid vessels has been performed.

Results

Newborns from mothers with bad eating habits had significantly higher values of the right carotid artery intima-media thickness /CAIMT/ ($p=0.046$).

Eating habits and Echo imaging

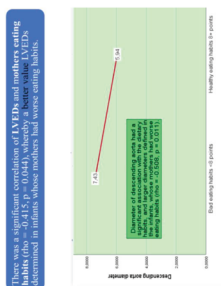
t-values are shown as median value with interquartile range; *p* – probability with level of significance set on $p < 0.05$

Parameter	Estimate (95% CI)	Standard Error (95% CI)	p
Intercept	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)	0.000
Age	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)	0.000
Gender	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)	0.000
Education	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)	0.000
Income	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)	0.000
Health	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)	0.000
Marital	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)	0.000
Religion	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)	0.000
Occupation	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)	0.000
City	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)	0.000
State	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)	0.000
Country	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)	0.000
Time	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)	0.000
Constant	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)	0.000

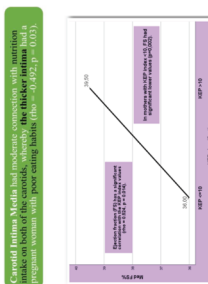
The correlation between KEP and Cardiovascular Variables

Correlations		
Variable	Coefficient	KEP index
RCA	ρ	-0.693*
	ρ	0.0047
A wave m/s	ρ	.424*
	ρ	0.044
FS%	ρ	.524*
	ρ	0.01

Only significant correlations are shown



There was a significant correlation of LVEDs and mothers eating habits ($r = -0.415$, $p = 0.044$), whereby a better value LVEDs determined in infants whose mothers had worse eating habits.



Carotid Intima Media had moderate connection with nutrition intake on both of the carotids, whereby the thicker intima had a pregnant woman with poor eating habits (rho = -0.492, $p = 0.03$).

Conclusions

Dietary eating habits and oral health of pregnant woman have significant connection with some segments of cardiovascular system development. Eating habits have an impact on diameter of blood vessels and on flow. Unhealthy dietary plans will most probably led to bad oral health and presence of periodontitis, which could contribute to the CAIMT and the development of atherosclerosis.

References & Acknowledgements

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