

Snežana Lešović*

CLINICAL AND LABORATORY FINDINGS IN ADOLESCENTS IN "CIGOTICA" PROGRAMME FROM 2008 TO 2012

INTRODUCTION: Obesity is becoming an increasingly important public health problem due to a drastic increase in its frequency, not only in adult but also at the pediatric and adolescent age, which directly and indirectly influences population morbidity, life expectancy and mortality. In response to the obesity epidemic in Serbia in 2008, the Center for the prevention, treatment and rehabilitation of obesity in children and adolescents was formed as well as "CIGOTICA" Programme at the Special Hospital "Zlatibor". The characteristics of programs "CIGOTICA" Programme is a multidisciplinary approach to the treatment of obese children, which includes specific training, dietary intervention with the reduction of total daily caloric intake, physical activity, clinical control and psychological support, change in behaviour and lifestyle.

OBJECTIVE: To identify the complications of obesity and metabolic risk factors in adolescents participating in CIGOTICA Programme.

METHOD: Anthropometric, clinical and biochemical parameters were analyzed in 1,000 adolescents (468 girls and 532 boys), of average 15.30 years of age (range 12 to 18) with primary obesity. The research was conducted at the Center for the Prevention and treatment of obesity in children and adolescents at the Special Hospital "Cigota" from 27 July, 2008 to 1 January, 2012. Hospitalization lasts 21 days. The criterion for obesity is the body mass index (BMI) > +2 SD. In addition to clinical examination, blood pressure was measured. Triglycerides, total, HDL and LDL cholesterol, uric acid and glucose were measured on the second day of hospitalization after 12 hours of fasting.

* Prim. Dr. Snežana Lešović M.Sci, Special Hospital for pediatric thyroid disorders and metabolic diseases Zlatibor, e-mail: @lsnez eunet. rs

RESULTS: Abdominal obesity defined as OS> P90 was diagnosed in all examinees (100%). 28% of adolescents had hypertension. Acanthosis nigricans was present in 51.4% of adolescents. Triglyceride values were high in 7.8% of patients, lower levels of HDL h were observed in 22.9% of the examinees, and high cholesterol was present in 5.8% of patients. Two risk factors for metabolic syndrome were observed in 27.6%, and metabolic syndrome was present in 18.3% of patients. 8.9% examinees had a glucose disorder (0.3%). Orthopedic complications were observed in 82% of the examinees. Polycystic ovary syndrome were observed in 12% of adolescents.

CONCLUSION: Complications occur in a large number of obese adolescents, which indicates the seriousness of the problem of obesity and the need for more effective prevention programmes. Short-term effects of Cigotica programme are encouraging, and the effectiveness of the multidisciplinary approach to obesity treatment will be evaluated by the current research which analyses sustainability of the achieved results.

Key words: obesity, adolescents, metabolic risk factors, insulin resistance, body mass index (BMI), CIGOTICA Programme

Introduction

Obesity in children is one of the biggest public health problems in the 21st century, with particularly alarming trends in some parts of the world. Various studies in Europe estimate that 10-30% of children aged 7 to 11 and 8-25% of adolescents aged 14 to 17 are overweight. In 1948, the World Health Organization declared obesity as a disease, and it now estimates that by 2025, 50% of the world population will be obese. Contemporary findings indicate an increase in the incidence of obesity in children and adolescents, with the particularly alarming findings that say that obese children develop more serious degrees of obesity and that up to 85% of obese adolescents are obese in adulthood (1).

Heredity, family environment, socio-economic and cultural conditions and daily habits influence the occurrence of obesity, and emphasize their mutual interactions (2). Concern about obesity in children is especially justified by the possibility of prevention of complications due to obesity, whose treatment is demanding, difficult, and often not so successful (3). Programmes to prevent obesity are becoming increasingly important because of the limited possibilities for its pharmacological and surgical treatment especially at the pediatric age (4.5).

Obesity in children is associated with an increased risk of a number of metabolic complications such as insulin resistance, impaired glucose tolerance and type 2 diabetes. Elevated BMI (body mass index) in childhood is a major generator of metabolic

syndrome. Obese children are at increased risk of orthopedic, respiratory illnesses and psychological problems (4). In addition to numerous complications, obesity is a cause of great economic loading through the reduction in productivity and income, and it accounts for 7-12% of all health care costs in Western countries (6).

The prevalence of obesity in Serbia in children up to five years of age is 19% according to the UNICEF office from 2005. According to the estimates for 2007, overweight and obesity are present in 18% of adolescents, and compared to the incidence in 2000, this shows an increase of almost 50%. Due to the continuous growth in the number of obese children in Serbia, and in order to prevent obesity and ensure changes in dietary habits and lifestyle, the Association of Pediatricians of Serbia, in cooperation with the Special Hospital "Zlatibor" that has years of experience in the treatment and rehabilitation of obesity in adults, in July 2007 prepared the project "Prevention and treatment of obesity in children and adolescents in Serbia." In the spring of 2008, the Republic Institute for Health Insurance under the auspices of the Ministry of Health approved the treatment and rehabilitation of obese children aged 12 to 18 for the period of 21 days once a year and the establishment of the Center for the Prevention, Treatment and Rehabilitation of overweight and obese children and adolescents in the complex of the Hospital "Zlatibor". Upon the decision of the Republic Institute for Health Insurance from May 2012, the treatment of obese children at the Center lasts for 10 days.

The Center performs diagnostic tests and treatment, with the participation of: a pediatric endocrinologist, a specialist in physical medicine, psychologists, nutritionists, physical education teachers and nurses. Once in three months, professors of pediatrics – endocrinologists from Belgrade and Nis visit the Centre to do consulting. Under professional supervision, patients receive a plan of eating and physical activity depending on their age, health and fitness, and if necessary, medication treatment is also included in the therapy. The immediate goal of the treatment is to achieve a long-lasting reduction in body-weight.

The treatment in CIGOTICA Programme requires a multidisciplinary approach that includes specific training, dietary intervention with a reduction in total calorie intake, physical activity, clinical and psychological support and changes in behavior and lifestyle. Upon admission, clinical examination identifies patients with primary and secondary obesity and complications, diagnostic procedures are planned, a diet and exercises are planned individually for each obese child. When leaving hospital, each child receives advice, guidance and recommendations for the supervision of a competent pediatrician.

The basic principle of nutrition for obese children and their families is taking balanced meals, which provide for the nutritive needs of a growing and developing body. Restriction of caloric intake in children is individualized and carefully monitored so as not to compromise normal growth and development (7,8). The total daily amount of food is distributed in 5 meals (breakfast, lunch, dinner, and 2 snacks). All

dishes are prepared in the kitchen of the Hospital "Zlatibor" under the supervision of experienced chefs and nutritionists. Meals are prepared in accordance with the basic principles and guidelines on the importance of proper nutrition in the prevention of obesity, based on initial daily caloric requirements and physical activity of children. Nutritionists' lectures and workshops are dedicated to the right choice of food, meal preparation, assessment of nutritional and caloric value of a meal, and upon release, children and parents receive written instructions and recommendations for the nutrition of obese children and adolescents.

CIGOTICA programme contains six types of physical activities, lectures and target programmes of social and entertainment activities. Health program activities are planned on the basis of the anaerobic capacity test. The planned physical activities are: walking, fast walking in the countryside, on the running track or in the cardio-fitness gyms, shaping exercises, exercises to strengthen certain muscle groups without props and accessories (therapeutic balls, elastic bands ...), exercises in water, swimming practice, field games, outdoor activities and sports games. Physical activity is organised on a daily basis, it is diverse, fun and tailored to obese children. Together with a hypocaloric diet, physical activity contributes to the reduction in weight, improvement of physical fitness, children are ready to engage in the standard programme of physical education, they are motivated to improve their health, and the greatest role is in maintaining the initially reduced body weight (9, 10).

Psychological treatment in the programme includes an interview with a psychologist, and a self-assessment questionnaire for psychological help, 6 workshops and assistance in understanding and solving the problem of obesity. Therapy programme that includes behavior modification gives much better results, and only a change of lifestyle can achieve long-term success. Therefore, for successful and long-term effects of the therapy in children, a psychological approach aimed at changing attitudes, beliefs and behaviors related to nutrition and physical activity is needed (11).

Lectures, workshops of pediatricians, nutritionists, psychologists, and physical education teachers together with obese children sharing their experiences, contribute to the adoption of new knowledge and attitudes towards the importance of proper nutrition (healthy eating choice in the selection of food, reducing meals), physical activity, improvement of interpersonal relationships and resolution of emotional problems in obese adolescents.

Objective

To determine the presence of complications of obesity and metabolic risk factors in adolescents participating in CIGOTICA programme.

Method

A prospective analysis was performed in 1,000 obese adolescents (468 girls and 532 boys), of the average age of 15.3, participants in "ČIGOTICA" programme, who were diagnosed with primary obesity. Obese children between the ages of 12 and 18 were hospitalized for 21 days in the special hospital "Čigota" for obesity treatment, education and rehabilitation in the period from 27 July, 2008 to 1 January, 2012. Adolescents diagnosed with secondary obesity, with medication therapy, unmotivated and adolescents who were hospitalised for less than 21 days were excluded from the research. Clinical monitoring of obese teenagers includes an initial overview, a survey on the diet and physical activity level, anthropometric measurements, ECG followed by an introduction to the basic principles of treatment and continuous monitoring of the patient. Body weight index BMI, fat % were obtained using a Tanita scale to determine body composition by impedance. While measured, a child should be in their underwear. Measuring is performed in the morning before breakfast and after emptying the bowel and bladder. The obtained value is read to the nearest 0.1 kg and is expressed in kilograms (one decimal place), and the weight of underwear is subtracted from it.

Body mass index (BMI) is obtained when the value of body weight in kilograms is divided by the square value of body height expressed in meters. The obtained results are expressed as the number of standard deviations through deviation (SD) of the reference values for a given age presented as Z-score and recommended by the WHO (National Center for Health Statistics-NCHS) WHO Growth Reference. According to recommendations, z-score values that indicate overweight and obesity are in the range of +2 to +3 SD and greater than +3 SD (12). Body height is measured by anthropometre with a stand. While measured, a child should be barefoot and bareheaded, his back to the bar of the anthropometre, with his head elevated so that the bottom edge of the orbit and tragus are in the same horizontal plane. The horizontal slider of the anthropometre in the measurement goes down to the scalp, and the height value is read to the nearest 0.5 cm, and is expressed in centimetres (to one decimal place). Circumferences (waist, hip, upper arm and thigh) are measured with a non-elastic plastic tape measure. The values are read to the nearest 0.1 centimeter and expressed in centimeters. Blood pressure is measured three times in a sitting position on the right arm, with an appropriate cuff. Triglycerides, total, HDL and LDL cholesterol, uric acid, and glucose are measured on the second day of hospitalization after 12 hours of fasting. The type and duration of each activity within ČIGOTICA programme were controlled on a daily basis. For the diagnosis of metabolic syndrome, IDF criteria (International Diabetes Federation) were used.

Results

From 27 July, 2008 to 1 January, 2012, 1,900 patients were hospitalized at the Center. A sample of 1,000 adolescents with primary obesity, average age 15.30 ± 1.45 was determined. Hospitalization lasted 21 days. Abdominal obesity defined as $OS > P90$ was observed in all patients (100%). Blood pressure was elevated in 290 patients (29%). Systolic hypertension was registered in 180 adolescents (18.00%), diastolic in 95 (9.50%), and systolic and diastolic in 91 (9.1%) adolescents. Clinical examination showed the presence of acanthosis in 514 adolescents: 265 girls (26.50%) and 249 boys (24.9%). In 51.4% of obese children, acanthosis was present in the neck, armpits, groin, and rarely on the flexor surfaces of the knees and elbows.

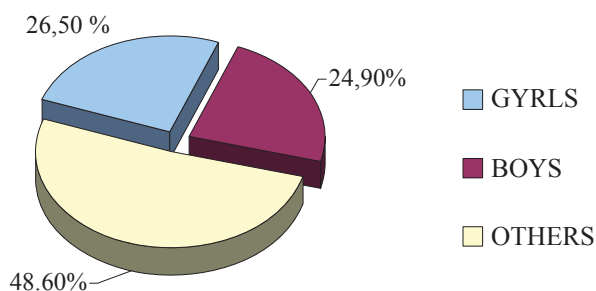


Figure 1. Acanthosis nigricans in the participants of CIGOTICA programme

Levels of triglycerides ($> 17 \text{ mmol/l}$) were elevated in 78 subjects (7.8%), lower levels of HDL ($< 1.00 \text{ mmol/l}$) were observed in 229 patients (22.9%) and high cholesterol was present in 58 adolescents (5.8%). Disorders in the regulation of glucose were detected in 95 (9.5%) patients, of which 61 (6.1%) had increased fasting glucose. Type 2 diabetes was detected in 3 adolescents (0.3%).

The criteria for the metabolic syndrome were met by 185 subjects (18.5%). Two risk factors for metabolic syndrome were observed in 282 patients (28.2%). One risk factor ($OS > p90$) for the metabolic syndrome was present in all patients. 39% (390) of adolescents had elevated levels of uric acid and microalbuminuria was not determined in all patients. Orthopedic complications were observed in 82% of the examinees. Polycystic ovary syndrome were observed in 12% of adolescents.

Discussion:

The alarming spread of the epidemic of obesity in children and adolescents, as well as the lack of reliable and effective policies and programs to prevent obesity indicate the need for the establishment of the Centre for the Prevention, Treatment and Rehabilitation of obesity in children and adolescents and CIGOTICA Programme at the Special Hospital "Cigota". Overweight and obese children aged 12 to 18 from school dispensaries and pediatric departments throughout Serbia are sent to the Centre.

Urbanization, industrialization, globalization of markets and economic growth have influenced the rapid change of lifestyle and diet ("nutritional transition"). Increased consumption of food with high energy density and high consumption of fat, especially saturated fat, and consumption of complex carbohydrates, vegetables and fruits along with sedentary life and lower energy expenditure, have significantly contributed to the rise of obesity in our society.

Blood pressure was elevated in 290 patients (29%). The connections between hypertension and obesity were noticed a long time ago. In both diseases, there are similar disorders in blood pressure that can trigger or maintain hypertension. Children with hypertension may have a disorder of glucose tolerance, preprandial or postprandial hyperinsulinemia or insulin resistance. Insulin stimulates the activation of the sympathetic nervous system, renin-angiotensin-aldosterone system and increases the re-absorption of sodium in the proximal renal tubules (13). Many epidemiological studies showed a distinct correlation between obesity and hypertension in children (14, 15). A research in Canada in 2012, suggests that obese boys have by 7.6 mmHg higher blood pressure compared to their peers with normal weight. Obese children who do insufficient physical activity, and have a positive family history of hypertension are at risk of hypertension. Early interventions in the treatment of obese children will reduce the number of obese children with hypertension, and the risk of cardiovascular diseases in the future (16).

Clinical examination showed the presence of acanthosis in the neck, armpits, groin, and rarely on the flexor surfaces of knees and elbows in 514 adolescents (51.4%). Acanthosis is a skin lesion that is characterized by hyperpigmentation and hyperkeratosis on the folding surfaces, followed by a rough and wrinkled skin (17). Pathological changes are present in the epidermis and are characterized by papillomatosis, hyperkeratosis, and increased number of melanocytes (18). Acanthosis is present in the clinical conditions associated with decreased insulin action at the cellular level, caused by genetic defects, insulin resistance induced most often by antireceptory antibodies, as well as by the pathogenetically insufficiently explained states of insulin resistance present in obese patients(19,20).



Acanthosis nigricans is an important predictor of insulin resistance in obese adolescents. Early identification of children with acanthosis (screening?), their monitoring and multidisciplinary treatment of obesity is essential for the prevention of complications, especially type 2 diabetes in children. Other changes registered in the skin of obese adolescents are Striae, acne, fungal infections of the skin, intertriginous changes, hyperpigmentation and hirsutism.

Obesity is a major risk factor for cardiovascular disease in adulthood. Undesirable effects of obesity are reflected at an early age in the changes in the lipid profile. Levels of triglycerides ($> 17 \text{ mmol / l}$) were high in 78 subjects (7.8%), lower levels of HDL ($< 1.00 \text{ mmol / l}$) were observed in 229 patients (22.9%) and high cholesterol was present in 58 adolescents (5.8%). The research of the National Health and Nutrition Examination Survey (NHANES) from 1999 to 2006, suggested that the prevalence of dyslipidemia in children aged 12 to 19 was 20.3%. Most of the complications of obesity are identified in adult patients, but some of them are already evident in children. The data from Bogalusa study showed that nearly 20% of obese children had at least one risk factor for cardiovascular diseases (hypercholesterolemia, hyperinsulinemia, hypertriglyceridemia, and hypertension) associated with the early onset of atherosclerosis. Insulin resistance is the most common metabolic disorder in obese children (21).

Increased prevalence of obesity in children and adolescents is associated with a higher risk of developing type 2 diabetes mellitus. Disorders in the regulation of glucose were detected in 95 (95%) patients. Type 2 diabetes was detected in 3 adolescents (0.3%). A disorder in the regulation of glucose indicates the risk of the disease. Obesity and insulin resistance in children makes them predisposed to vascular complications in later life. Severe obesity at the age of 9-11 leads to the reduction in carotid artery elasticity and obesity in adolescence leads to the thickening of the intima-media carotid arteries in young adults (22). Bogalusa study showed that the prevalence of fibrous plaques in the aorta and coronary arteries increases with age and positively correlates with BMI z-score, triglyceride and cholesterol levels and blood pressure. Elevated BMI in childhood is a major generator of metabolic syndrome, which is

characterized by: abdominal obesity, glucose intolerance, insulin resistance, dyslipidemia (low HDL cholesterol and triglycerides), hypertension, chronic inflammation, and prothrombotic states. Metabolic syndrome increases the risk of diabetes and cardiovascular mortality. Approximately 24-51% of obese children between the age of 12 and 19 have metabolic syndrome. The prevalence of metabolic syndrome is significantly lower in normal weight adolescents (1-3%) compared with the obese adolescents in the United States.

The criteria for the metabolic syndrome are met by 18.3% of our respondents. Two risk factors for metabolic syndrome are observed in 28.2% of adolescents. One risk factor (OS > p90) for the metabolic syndrome is present in all patients. The accumulation of abdominal subcutaneous and visceral fat is associated with insulin resistance, and insulin sensitivity correlates less with femoral and gluteal subcutaneous fat. The accumulation of visceral fat is accompanied by resistance to the action of adipose tissue insulin sensitivity and increased catecholamines. These patients are at high risk of cardiovascular diseases and type 2 diabetes in adulthood (23, 24). Ever since risk factors for metabolic syndrome were identified, there has been a need for screening obese children who have two or more risk factors, in order to try to prevent the development of complications and start the treatment.

39% of adolescents have elevated levels of uric acid and microalbuminuria is not determined in all patients. Obesity is a risk factor for chronic renal failure. The first sign of kidney damage is microalbuminuria. Kidney damage is caused primarily by hemodynamic and hormonal changes in obese children and secondarily, occurs with type 2 diabetes and hypertension (25).

In addition to these complications of obesity, our patients have liver steatosis, steatohepatitis, rapid growth, ovarian hyperandrogenism in girls and gynecomastia in boys, cholecystitis, holecistiasa, pancreatitis, sleep apnea, stress incontinence. Orthopedic complications and problems of the bone and joint system are present in obese adolescents. Anamnestic data indicate frequent injuries and fractures in our obese adolescents, who most often complain of pain in the hips, knees and feet. 82% of obese adolescents have one of the changes in the osteoarticular design trails: spinal deformity, varus knees or flat feet. Three patients had epiphyseolysis femoral head, and two of them had Blount disease. It is necessary to identify orthopedic complications in obese children as soon as possible and encourage them to get involved as soon as possible in alternative forms of physical activity (trekking, swimming ...). (26).

Menstrual disorders with insulin resistance, acne, hirsutism and *akanthosis nigricans* are characteristics of the polycystic ovary syndrome, which is also present in 56 (12%) our obese adolescents.

Psychological problems and often psychological consequences of obesity: anxiety, phobias, depression, aggression, abuse of tobacco in our patients indicate the fact that in the treatment psychological help and support are also needed (27).

The need for the prevention of obesity stems from a dramatic increase in its incidence, limited treatment options and the direct and indirect impact on the development of a number of chronic diseases that occur with obesity at the young age. Obesity is associated with significant health problems in the pediatric population and is an important risk factor for morbidity and mortality in adulthood. Therefore, finding ways to reduce the growing prevalence of its sequels in children and adults is a challenge. Obesity prevention should begin in early childhood, focusing on healthy eating and physical activity (28).

The effects of CIGOTICA are encouraging and indicate that the multidisciplinary approach has led to a significant reduction in body weight, normalization of blood pressure and metabolic risk factors, increased aerobic capacity and self-esteem in obese adolescents.

Conclusion

Complications occur in a large number of obese adolescents, which indicates the seriousness of the problem of obesity and the need for more effective prevention programmes. The multidisciplinary approach in the CIGOTICA programme treatment leads to a significant reduction in body weight, improvement in metabolic risk factors, aerobic capacity and self-esteem among adolescents. The effectiveness of CIGOTICA and the multidisciplinary treatment of obese adolescents will be evaluated by the current research that examines sustainability of the achieved results.

References

1. Weiss R, Caprio S. Obesity in children and adolescents. *J Clin Endocrinol Metab* 2008; 93 (11): 31-6.
2. Caprio S, Weiss R. The metabolic consequences of childhood obesity. *Best Practice and Research Clinical Endocrinol Metab* 2005; 19 (3): 405-19.
3. Comuzzie AG, Allison DB. The search for human obesity genes. *Science* 1998, 280: 1374-7.
4. Anemiya K, K Duhashi, Unkam T, Sugihara S, T Obzeki, Tajin N. Metabolic syndrome in youth. *Pediatric Diabetes* 2007; 81st DH Bessesen Update on Obesity. *J Clin Endocrinol Metab* 2008; 93:2027-34.
5. Guo SS, Wu W, Chumlea WC, Roche AF, Predicting overweight and obesity in adulthood from body mass index values in childhood and adolescence. *Am J Clin Nutr* 2002; 76: 653-8.
6. Hammond R, Levine R. The economic impact of obesity in the United States. *Diabetes Metabolic Syndrome and Obesity Targets and Therapy* 2010, 3: 285-295.
7. Maffei C, Banzato C, Talamini G. Waist-to-Height Ratio, a Useful Index to Identify High Metabolic RISIKA in Overweight Children. *J Pediatr* 2008; 152: 207-13.

8. Anne E. Matthews. Children and obesity: a pan-European project examining the role of food marketing. *Eur J Public Health* 2008, 18: 7-11.
9. Ludwig SD. Childhood obesity-shape of the thing it came. *N. Engl J Med* 2007; 357: 3225-27.
10. RS Stender, Burghen GA, JT Mallare. The role of health care providers in the prevention of overweight and type 2 diabetes in children and adolescents diabetic, *Spectrum* 2005, 18: 240-8.
11. Dianne Neumark Sztainer, Jess Haines, Ramona Robinson-O'Brien, Peter J. Hannan, Michael Robbins. Obesity prevention program for children: a feasibility study *Health Educ. Res* 2009, 24: 407-20.
12. WHO Child Growth Standards 2006: Length / height-for-age, weight-for-age, weight-for-length/weight-for-height and body mass index-for-age. Methods and development. Available at: [http // www.who.int / childgrowth / en](http://www.who.int/childgrowth/en). Retrieved 15.01.2009.
13. Sen Y, Kandemir N, Alikasifoglu And Gone N, Ozon A. Prevalence and risk factors of metabolic syndrome in obese children and adolescents the role of the severity of obesity. *Eu J Pediatr*, (Epub, ahead of print), 2008.
14. Freedman DS, Dietz WH, Srinivasan SR, Berenson GS: The relation of overweight to cardiovascular risk factors among children and adolescents: the Bogalusa Heart Study. *Pediatrics* 1999, 103: 1175-1182.
15. Sorof J, Daniels S: Obesity hypertension in children: a problem of epidemic proportions. *Hypertension* 2002, 40: 441-447.
16. Yipu Shi, Margaret de Groh and Howard Morrison. Increasing blood pressure and its associated factors in Canadian children and adolescents from the Canadian Health Measures Survey Shi et al. *BMC Public Health* 2012, 12: 388
17. Schwartz RA. Acanthosis nigricans. *J Am Acad Dermatol* 1994; 31: 1-19.
18. DL Rogers. Acanthosis nigricans. *Semin Dermatol* 1991, 10: 160-3.
19. Torley D, Bellus GA, Munro CS. Genes, growth factors, and acanthosis nigricans. *Br J Dermatol* 2002; 147: 1096-101.
20. Eberting CL, Javor E, Gordon P, Turner ML, Cowen EW. Insulin resistance, acanthosis nigricans, and hypertriglyceridemia. *J Am Acad Dermatol* 2005, 52: 341-4.
21. Gerald S. Berenson, MD, Wendy A. Wattigney, MS, Richard E. Tracy, MD, PhD, William P. Newman III, MD, R. Sathanur Srinivasan, PhD, Larry S. Webber, PhD, Edward R. Dalferes Jr., BS, Jack P. Strong, MD. Atherosclerosis of the aorta and coronary arteries and cardiovascular risk factors in persons aged 6 to 30 years and studied at necropsy (the Bogalusa Heart Study). *The American Journal of Cardiology*, Volume 70, Issue 9, 1 October 1992, Pages 851-858.
22. Baker JL, Olsen Lina W, Sorensen TIA. Childhood body-mass index and the risk of coronary heart disease in adulthood. *N Engl J Med* 2007; 357: 2329-37.
23. Klein S, Romijn JA. Obesity. *U Kronenberg : Williams Textbook of Endocrinology*, 11th ed. Saunders, Philadelphia, 2008; 1563-80.
24. Haug T, Nansel TR, AR Belshe, Morrison JA. Specificity, and Predictive Values of Pediatric Metabolic Syndrome in Relation to Component Adult Metabolic Syndrome: The Princeton LRC Follow-up Study. *J Pediatr* 2008; 152: 185-90.

25. Morales E, Vlaero A, Leon M et al. Beneficial effects of weight loss in overweight patients with chronic proteinuric nephropathies. *Am J Kidney Dis* 2003, 41: 319-27.
26. Erica D. Taylor, R. Kelly Theim, Margaret C. Mirch, Samareh Ghorbani, Marian Tanofsky-Kraff, Diane C. Adler-Wailes, et al. Orthopedic Complications of Overweight in Children and Adolescents *Pediatrics* June 2006; 117:6 2167-2174;
27. Dawn K. Wilson. New Perspectives on Health Disparities and Obesity Interventions in Youth. *J Pediatr. Psychol.* 2009, 34: 231-44.
28. Baničević M, Zdravkovic D, Mitić D, Curčić V. Medical Center Regulations for prevention and treatment of obesity in children and adolescents. Zlatibor: Special hospital for thyroid disorders and metabolic diseases, 2008.