

## STATEMENT

**By:** Professor Daniela Mircheva Avdjieva-Tzavella, MD, PhD, Department of Clinical Genetics, University Pediatric Hospital, Medical University-Sofia,  
Member of a Scientific Jury according to the Order of the Rector of Medical University - Varna - R-109 –270/05.08.2024

**Regarding:** dissertation "Bone health and fracture risk among peripubertal and adolescent children: the importance of body weight, adipose tissue distribution and the presence of metabolic abnormalities" for the award of the educational and scientific degree "Doctor" to Dr. Veselin Milkov Boyadzhiev

Field of higher education: 7. Health and Sport; Professional Field 7.1 Medicine; Scientific specialty "Paediatrics"

Form of doctoral studies: independent, Department of Paediatrics at the Medical University of Varna

Scientific supervisor: Prof. Dr. Violeta Iotova, PhD and Prof. Dr. Boryana Varbanova, PhD, Department of Pediatrics, Medical University - Varna

### **Biographical data about the PhD student**

Dr. Veselin Boyadzhiev graduated in medicine at the Medical University - Varna in 1999. Since 2001 he has been working at the First Pediatric Clinic of the University Hospital " St. Marina". Since 2001 he is also an assistant at the Clinic of Pediatric Endocrinology at the Department of Pediatric Diseases and Medical Genetics of MU - Varna, chief assistant 2011-2015, administrative assistant since 2014. He has acquired specialties in Pediatrics (2005) and Pediatric Endocrinology (2009). Member of the Bulgarian Pediatric Association, Bulgarian Society of Pediatric Endocrinology and Varna Society of Pediatric Endocrinology. He has participated in three projects, one of which - "Prospective, multicentre, single-arm study to evaluate efficacy, safety and pharmacokinetics of Denosumab in children with osteogenesis imperfecta" is the principal investigator. He has participated in numerous courses in pediatric endocrinology, growth disorders and bone dysplasias.

The dissertation submitted for my opinion is structured in accordance with the Academic Staff Development Act in the Republic of Bulgaria (ASDA). The dissertation comprises 147 standard pages of which 124 pages are main text and contains all the main sections - introduction (1 p.), literature review (36 p.), hypothesis, aim and objectives (1 p.),

research design and methods (8 p.), results (51 p.), discussion, conclusions and contributions (27 p. in total). The reference list includes 463 sources, all in English. The dissertation contains 75 figures and 50 tables.

### **Relevance of the topic**

Fractures in childhood is a particularly common pediatric problem - about 1/3 of all children fracture at least once during the period of childhood, the percentage in boys can reach up to 50%. They have a bimodal distribution, which in both sexes has a first peak around 6-7 years of age and a second later peak during puberty. In recent years, much new knowledge has accumulated in the biology of growing childhood bone, many of the genetic and molecular mechanisms involved in the regulation of normal skeletogenesis have been revealed, it has become clear that bone is a complex system actively involved in general metabolism, that adipose tissue is actively involved in the regulation of bone metabolism, and obesity is a new and recently recognized risk factor for bone strength disorders.

In this context, this dissertation is relevant. It presents the first Bulgarian study on the epidemiology of childhood fractures and bone densitometric indices among overweight and obese girls, attempting to determine the influence of body weight, body composition, and the presence of metabolic abnormalities on the processes of bone maturation and the attainment of optimal bone strength in late childhood. Disturbances in normal bone growth and failure to achieve adequate bone strength during childhood may be a serious prerequisite for increased risk of developing early osteoporosis and increased fracture risk in adulthood.

### **Knowledge of the problem**

The literature review is detailed and informative, based on 380 sources, and shows a thorough and comprehensive knowledge of the issue. The focus is mainly on the biology of growing children's bone, methods of assessing bone parameters and body composition, osteoporosis in childhood, epidemiology of fractures in childhood and adolescence, osteometry and fracture risk, obesity and fracture risk, and the influence of adiposity and metabolic abnormalities on bone.

The aim of the dissertation is clearly formulated as establishing the epidemiological characteristics of fractures among the pediatric population of the town of Varna and the study of bone densitometric indices among overweight and obese girls by determining the influence of body weight, body composition, amount of visceral adipose tissue and the presence of



metabolic abnormalities on the processes of bone maturation and the achievement of optimal bone strength in late childhood. The set objectives are in line with the aim of the study.

### **Methodology of the study**

The study was conducted in two separate phases. In the first stage, a survey of 2,513 students aged 16 to 19 was conducted in 14 secondary schools in Varna during the period 2021-2022. The second, clinical part of the study was conducted on the territory of the University Hospital "St. Marina" - Varna in the period January 2023 - January 2024. It included 41 girls aged between 14 and 17 years who were hospitalized in connection with overweight, disturbances in carbohydrate metabolism, menstrual disorders or the presence of bone and joint complaints. Patients in the clinical arm of the study underwent a thorough history taking, anthropometric measurements and a thorough physical examination. A number of laboratory (CBC, general biochemical panel, lipid profile, calcium-phosphorus metabolism, OGTT glycated hemoglobin, urinalysis) and instrumental (DXA densitometry of bone parameters and body composition, wrist, hand and finger radiographs, abdominal ultrasonography, bioelectrical impedance analysis) investigations were performed.

The methods listed are presented in detail and suitably illustrated. The methodology thus presented is stable, logical and allows reliable results to be achieved in response to the stated objective.

### **Evaluation of the thesis and contributions**

In the dissertation for the first time in Bulgaria it is made:

A study on the epidemiology of fractures in childhood;

Study and analysis of DXA densitometric indices of visceral adipose tissue quantity and determine the correlations of visceral adipose tissue with bone health among adolescents;

Detailed analysis of body parameters and their relationship to metabolic abnormalities, demonstrating the leading influence of fat and fat-free body mass on bone growth during adolescence.

Of practical value are the results of the present study, pointing to a worsening of bone deficiency with advancing degree of obesity. This calls for the introduction of routine screening osteometric examinations into clinical practice, especially among adolescents with high-grade and extreme obesity. Data from bioelectrical impedance analysis to determine body composition suggest that, for clinical practice, this may be a novel, efficient and highly

informative method for the diagnosis and follow-up of overweight and obese children and adolescents.

The discussion is done competently and adequately in accordance with the literature data from the bibliography used. The conclusions are logically drawn from the results obtained. Terms are used correctly, the text is structured logically correctly, figures and tables are of high quality and precise explanation.

The thesis therefore makes a strong practical contribution and represents a comprehensive and thorough study on the importance of body weight, adipose tissue distribution and the presence of metabolic abnormalities on bone health and fracture risk among peripubertal children and adolescents.

### **Autoreferat**

The autoreferat in 104 pages reflects the content of the thesis very well. Both the autoreferat and the main dissertation are richly illustrated with many colour figures and tables.

I have no significant criticisms of the dissertation submitted for my opinion.

### **Conclusion**

The dissertation contains scientific and applied results, which represent an original contribution to science and meet the requirements of the Law for the Development of Academic Staff in the Republic of Bulgaria (LADAB), the Regulations for the Implementation of the LADAB and the internal criteria of MU - Varna. The submitted materials and dissertation results fully comply with the specific requirements of MU - Varna.

The dissertation work gives me a reason to claim that the dissertant Dr. Veselin Boyadzhiev possesses in-depth theoretical knowledge, demonstrates high professionalism and skills to independently conduct in-depth scientific research.

Because of the above, I confidently give my **positive assessment** of the research conducted, presented by the above-reviewed dissertation, abstract, results and contributions, and **propose to the honorable scientific jury to award the educational and scientific degree of "Doctor" to Dr. Veselin Milkov Boyadzhiev in the doctoral program in the scientific specialty "Pediatrics"**.

14.10.2024 г.

Prof. D. Avdjieva-Tzavella

Заличено на основание чл. 5,  
§1, б. „Б“ от Регламент (ЕС)  
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