

OPINION

by Assoc. Prof. Dr. Milena Ivanova Belcheva

Department of Pediatrics, MU "Prof. Dr. Paraskev Stoyanov", Varna

Subject: Dissertation work for the award of an educational and scientific degree "**Doctor**"

Field of higher education: 7. "Health care and sports"

Professional direction: 7.1 Medicine

Doctoral program: Pediatrics

Form of doctoral study: Independent form of study

Author: Dr. Veselin Milkov Boyadzhiev, Department of Pediatrics, Faculty of Medicine, Medical University - Varna.

Topic: „Bone health and fracture risk among peripubertal and adolescent children age - importance of body weight, distribution of fat tissue and the presence of metabolic disturbances”.

Scientific supervisors: Prof. Dr. Violeta Yotova, Ph.D. and Prof. Dr. Boryana Varbanova, d.m.

Scientific consultant: Prof. Dr. Dimitar Ivanov Raykov, MD.

General presentation of the procedure by order No. R-109-270/05.08.2024 of the Rector of the MU "Prof. Dr. Paraskev Stoyanov" Varna, based on the decision of the Faculty Council of the Faculty of Medicine (Protocol №25/29.07.2024). I was elected as an internal member of a scientific jury evaluating the dissertation work of Dr. Veselin Milkov Boyadzhiev on the topic: “Bone health and fracture risk among peripubertal and adolescent children – significance of body weight, the distribution of adipose tissue and the presence of metabolic disturbances”

On the basis of Protocol No. 1/16.08.2024 of the first meeting of the scientific jury I am determined to prepare an opinion. The set of materials provided by the doctoral student on the procedure for awarding of ONS "Doctor" is complete, it is available in electronic version and on paper carrier and is in accordance with the Regulations for the Development of the Academic Staff of the MU- Varna, as well as the Law on the Development of the Academic Staff in the Republic of Bulgaria.

Brief biographical data of the PhD student

Dr. Veselin Milkov Boyadzhiev graduated in medicine at the Medical University of Varna "Prof. Dr. Paraskev Stoyanov", in 1999. In 2001 he started working in Pediatric Endocrinology Clinic

at the Department of Children's Diseases and Genetics of the Medical University - Varna. From 2001 to the present, he holds the position of assistant, chief assistant, administrative assistant at the Department of Pediatrics of the Medical University of Varna. Acquired a specialty in pediatrics (2005) and pediatric endocrinology (2009 year). Meanwhile, Dr. Boyadzhiev participated in the teams of several international projects, including as principal investigator. He takes an active part in numerous congresses and conferences in pediatric endocrinology and specializes in the field of children's bone health, skeletal dysplasias and osteogenesis imperfecta in leading European centers. His research interests are in the field of childhood diabetes and bone diseases in children. He is a member of the Bulgarian pediatric association, the Bulgarian Society of Pediatric Endocrinology and The Varna Society of Pediatric Endocrinology. The doctoral student has excellent theoretical training, extensive practical experience, additional qualifications and targeted scientific and practical interests in the field of the doctorate.

Relevance and importance of the topic.

The present work is the first in our country to investigate the epidemiology of bone fractures and assesses the influence of overweight, obesity and metabolic risk on bone health indicators in children. The problem is extremely relevant given the rapid rate of growth of obesity among children, especially in our country and the accumulation of data on the multifaceted, including orthopedic, consequences of it. The reflection of adipose tissue on the construction, modeling and strength of bone in adolescents is a relatively new problem that is the subject of lively scientific interest. Deepening knowledge about interdependencies between fat and bone tissue during childhood has the potential to offer guidance for early intervention, oriented towards the full development of the bone system during childhood and preventing the development of early osteoporosis in the population. I find the chosen topic of the dissertation important, relevant and extremely useful for clinical practice.

Characterization and evaluation of the dissertation work.

The dissertation is well structured, following the classical structure with all the main parts presented, unfolded in a balanced way.

Literature review (36 pages): The literature review is presented on 36 pages, in-depth and focused on the scientific problem. The biology, physiology and structure of the growing are presented in detail bone and the causes of osteoporosis in childhood and adolescence. They are exhaustively described the place and importance of modern tools for osteometry and assessment of bone morphology, as well as body composition research methods. Modern epidemiological data on fracture risk in children are presented the light of their increasing obesity. Much of the literature review is dedicated to the influence of adipose tissue and its distribution on bone, the role of adipokines and

osteocalcin as mediators of the relationship between these tissues and the role of muscle mass in improving bone parameters.

The literature review provides a reasoned basis for the need to study of the epidemiology of fractures among Bulgarian children and the role of fat mass and metabolic disorders as a risk factor for bone health in overweight and obese girls.

Aim and tasks (1 page): A total of 8 tasks were set, 4 each for the epidemiological and the clinical part of the study, which are logical, clearly worded and in full compliance with the set objective.

Setting up own research (9 pages): The scientific research carried out is transversal (cross-section) in two different directions - epidemiological and clinical analysis. The selection of participants is done very carefully and allows obtaining good quality results. The analyzed target group is sufficient in number and makes statistical analysis possible. The grouping of female participants based on the degree of obesity and according the number of criteria for metabolic syndrome allows a detailed analysis of the complex relationships between bone strength and body composition, as well as the effect of metabolic effects. Research methods are described in detail and consistently and give a clear idea of the approach to the problem. It makes an impression the wide range of tools used and the efforts to standardize those obtained data. This allows solving the set tasks. All research is conducted prospectively. Worked with the permission of the Commission on Ethics of the scientific researches at MU-Varna.

Results (50 pages): The data analysis is very thorough and comprehensively covers all possible aspects of scientific issues. The results of the study are clear presented in 49 tables and 73 figures and presented in a coherent and clear text. They are divided into two parts. Epidemiological research determines for the first time in our country, the frequency of fractures among a large number of teenagers and girls outlines its epidemiological characteristics. It establishes an increased fracture frequency among overweight/obese children, especially in girls, which in the analysis of the target group finds its explanation with the effects of the amount of fat mass, its dilution and related metabolic factors on osteometric indicators. As a result of dividing the participants into groups according to the degree of obesity, an important conclusion is reached about the complex "biphasic" impact of the amount of fat mass and its characteristics on bone mineral density and indicators of bone health. At the same time, the results have been confirmed by using two tools – whole-body densitometric examination and bioelectrical impedance analysis. Very precisely the PhD student presents the positive correlation between whole-body bone mineral density and lean body mass

indices, as well as the impact on them of advancing obesity. The analysis of osteometric indicators of the lumbar vertebrae convincingly proves much more weak correlation with fat mass, fat-free mass and metabolic parameters impacts.

Finally, separate chapters present the results of the analysis of biochemical and hormonal effects, indicators of calcium-phosphorus metabolism and serum levels of vit. D.

Discussion (21 pages): Consequentially, following the logic of what has been done study Dr. Boyadzhiev presents a comparison of his scientific results with modern scientific knowledge. A parallel has been drawn with the results of numerous studies concerning all analyzed indicators. They make an impression the in-depth critical analysis of the publications from the rich bibliography and the own reasoned and competent interpretation of the doctoral student in relation to the established differences and similarities between studies.

Conclusions, contributions and conclusion (4 pages): Clearly, logically and accurately formulated a total of 16 conclusions - 5 for the epidemiological and 11 for the clinical part of the dissertation labor that are in agreement with the tasks set. All of them are brought up for the first time in the national scientific space. Based on the conclusions, 8 contributions were formulated with original, scientific-practical and confirmatory character.

Publications related to the subject of the scientific research: Dr. Boyadzhiev presents 5 publications (2 articles in Bulgarian and 3 participations in international conferences in English). In all of them he is the first author, which he confirms his personal contribution in developing the scientific concept, study design, the collection and summarization of the results and their publication.

Bibliography: The bibliography includes 463 literary sources in Latin. The analyzed scientific publications are contemporary and reflect current achievements in the field of scientific subject matter. Publications from the last 5 years are included an expression of continuing research interest in the topic.

Evaluation of the contributions of the dissertation work. The dissertation concludes with the presentation of 8 contributions that are significant and highlight the current dissertation as a solid foundation for upcoming scholarly work research. Some of them have a marked scientific-applied nature and set guidelines for follow-up and early intervention to protect bone health in girls with high and extreme obesity. I accept the contributions presented.

CONCLUSION

The dissertation work of Dr. Veselin Boyadjiev is dedicated to current scientific problem and contributes to the deepening of knowledge about the complex interactions between obesity and osteometric parameters in girls c childhood-adolescence, while setting guidelines for follow-up and early intervention to protect bone health in girls with high-grade and extreme obesity. In terms of structure, volume and content, the presented dissertation corresponds to all the requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria, The Regulations for its implementation and the Regulations of MU "Prof. Dr. Paraskev Stoyanov" - Varna for awarding the scientific and educational degree "Doctor". Dr. Boyadzhiev's dissertation reflects several years of in-depth research work thought out in detail and carried out competently and thoroughly by a complete clinician. It is an original development of the doctoral student and demonstrates his broad theoretical erudition, professional skills and developed qualities for analysis and synthesis of scientific information and conceptualization of scientific research. I give my positive assessment for the dissertation work on the topic "Bone health and fracture risk among peripubertal and adolescent children – importance of body weight, the distribution of adipose tissue and the presence of metabolic deviations" and I suggest the esteemed scientific jury to vote "yes" awarding of scientific and educational degree "Doctor" to Dr. Veselin Milkov Boyadzhiev.

04/11/2024

Reviewer:

Assoc. Prof. Dr. Milena Belcheva

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