

REVIEW

by Professor, Dr. Mihail Angelov Boyanov, Doctor of Medical Sciences,

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Member of the scientific jury according to Order P 109-270 / 05.08.2024 of the Rector
of the University of Varna

of a dissertation thesis for awarding the educational and scientific degree 'doctor'
professional direction Medicine and sports; doctoral program Pediatrics

Author: Dr. Veselin Milkov Boyadzhiev; Form of doctoral study: independent
preparation

Department: Pediatrics, Medical University "Prof. P. Stoyanov" - Varna.

Topic: BONE HEALTH AND FRACTURE RISK AMONG PERIPUBERT AND ADOLESCENT
CHILDREN - IMPORTANCE OF BODY WEIGHT, FAT DISTRIBUTION AND THE PRESENCE OF
METABOLIC ABNORMALITIES

Scientific supervisors: Prof. Dr. Violeta Yotova, MD; Prof. Dr. Boryana Varbanova, MD;
Medical University - Varna.

1. General presentation of the procedure and the doctoral student

Dr. Veselin Milkov Boyadzhiev has presented a set of materials on an electronic
medium, which is in accordance with Article 69 of Section 3.; Regulations for the
development of the academic staff of MU-Varna. The set includes a project for an abstract, a
dissertation, publications and scientific contributions - original and lists.

The doctoral student has attached 2 (two) full-text publications and 3 (three) scientific
contributions (posters).

2. Brief biographical data for the doctoral student

Dr. Veselin Milkov Boyadjiev completed his higher education in medicine at the
Medical University "Prof. Dr. Paraskev Stoyanov" - Varna in 1999. In 2001, he became an
assistant at the Department of Pediatrics at UMBAL "St. Marina" - First Children's Clinic, and
since 2011 he is the chief assistant. He has acquired 2 specialties: pediatric diseases (2005)
and pediatric endocrinology (2009). He frequented numerous short-term specializations in

leading foreign units, as well as participation in various scientific projects and clinical studies. A search of the SCOPUS database reveals data on 17 publications, at least 2/3 of which are original, as well as data on 271 citations and an h-index of 4.0.

3. Actuality of the topic and appropriateness of the set goals and tasks

The topic of the dissertation is the relationship between bone health (fracture frequency and bone mineral density, BMD) and body weight and composition in peripubertal and adolescent children. The relevance of this topic is indisputable. The initial notion of a beneficial effect of obesity on bone health in adults has gradually been disproved. Data have been accumulated on the relationship between adipose tissue, obesity, osteo-sarcopenia and bone health in adults, including in our country (for example, in the dissertation work of Dr. Martin Nikolaev Nikolov, Pleven 2023). Information concerning children and adolescents remains extremely scarce. And overweight and obesity are an epidemic on the rise among Bulgarian teenagers. Thus, the peer-reviewed dissertation fills a gap in scientific and practical knowledge.

4. Knowledge of the problem

The literature review on the topic under consideration covers 37 pages of the dissertation work (approx. 25%). Introductory data on the anatomy and physiology of bone growth in children and adolescents are reviewed in detail. Special attention is given to methods of assessing bone mass/density and body composition in this young population. The possibilities of supplementing the data from two-dimensional dual-energy X-ray absorptiometry are discussed. Other available bone assessment methods such as quantitative computed tomography, for example, are also reviewed. Extremely interesting and thorough is the section dedicated to osteoporosis in children and adolescents, which almost always has a genetic etiology, as is the case with osteogenesis imperfecta. Data on the epidemiology of fractures in children are presented. Particular attention is paid to the influence of different components of body composition on bone maturation in children and adolescents. The text is clear, specific and completely up to date. By presenting the problem in breadth and depth, the doctoral student has shown a thorough knowledge of previous scientific knowledge, on which he builds his hypotheses and scientific research.

In the literature review and whole text, 463 sources are cited, more than half of which are from the last decade. Important and reliable sources have been used, and a balance has

been sought between confirming and rejecting these scientific studies. As a certain weakness I consider the fact that there is not a single source by Cyrillic authors.

5. Research methodology

Based on the literature review, Dr. Boyadzhiev formulated as the goal of his research "To establish the epidemiological characteristics of fractures among the children's population of the city of Varna and to study the bone densitometric indicators among overweight and obese girls, determining the influence of body weight, distribution of body composition, amount of visceral fat and presence of metabolic deviations on bone maturation processes and the attainment of optimal bone strength in late childhood'. The 8 tasks focused on the epidemiological part (numbers 1-4) and the clinical part (numbers 5-8) follow logically from this goal.

The chosen research methodology is a cross-sectional, one-moment study in 2 parts:

- Epidemiological, including students aged 16 to 19 years, based on questionnaires on bone health and previous fractures;
- Clinical – in girls between the ages of 14 and 17, hospitalized due to overweight, deviations in carbohydrate metabolism, menstrual disorders or the presence of bone and joint complaints.

This combination allows achieving the set goal and obtaining an answer to the formulated tasks.

6. Characterization and evaluation of the dissertation work

The material and research methods are presented in 8 pages. The selection of epidemiological and clinical groups is clearly explained and properly conducted. The inclusion and exclusion criteria for participation were selected successfully. All the requirements from the point of view of the ethical norms for the participation of persons in studies have been met. The clinical examinations were carried out in the Clinic for Endocrinology and Metabolic Diseases, and the clinical-laboratory ones - in the Central Clinical Laboratory at UMBAL "St. Marina" - city of Varna. This has ensured the necessary quality control and modernity of the applied laboratory methods. Body composition and distribution were assessed by two independent methods – dual-energy X-ray absorptiometry (DXA) and bio-electrical impedance. Additional modern formulas and calculations were also

used to supplement the information from the two measurements. However, the expected errors of the two measurement methods are not specified.

The epidemiological study covered a total of 2,513 surveyed students, $\frac{1}{4}$ of them electronically. The clinical part included 41 girls, which is a relatively small number to obtain generally valid conclusions. Therefore, the results obtained in this part of the study should be considered rather as pilot (preliminary) and can become the basis for further expansion of scientific research in the field of research. The statistical methods are correctly selected, modern and allow reaching the statistical significance of the results even with the relatively small number of participants in the clinical part of the study.

The results are presented on a total of 51 pages, and the Discussion - on 22 pages. In total, the dissertation work includes 50 tables and 75 figures. Thus, the data are well illustrated, although the abundance of abbreviations would make it difficult for the less prepared reader.

In short, the data from the dissertation show a frequency of fractures in children similar to data from other European countries - 13.1%; with 30-40% of children with fractures having more than one. The role of body weight is also visible - with an increase in BMI and fat tissue, the risk of fractures in traumas increases.

In the clinical part, several important conclusions from a scientific and practical point of view are made. The so-called "stimulating" influence of adipose tissue on the bone system is present only up to a certain degree of obesity, after which this tendency disappears and even reverses. The dissertation concluded that the absolute bone mass in children with high degree of obesity is probably insufficient to meet the increased mechanical loads. Interesting data are also obtained for the bone mass and adipose tissue of the forearm. The dissertation describes an imbalance between muscle and adipose tissue in this area with a consequent deficiency in the growth of diameter bones - one of the leading causes of the observed increased incidence of forearm fractures.

In their entirety, the results are presented in a thorough, analytical and overview manner. This has allowed the dissertationer to develop a well-focused discussion of the results obtained. Various aspects of the study are commented on and comparisons with similar studies in other countries and populations are cited. The part summarizing the relationship of hormonal and metabolic indicators with bone indicators and bone strength is also of interest. Thus, well-chosen comparisons with other authors have allowed the doctoral student to formulate generalized conclusions that clearly reflect the essence of the dissertation work, although in their characteristics they partially repeat the main results. It

would be helpful if they ended with some practical direction or suggestion for further research.

7. Contributions and significance of the development for science and practice

The dissertation contains several scientific and scientific-applied achievements. Significant new aspects of existing scientific problems are proved by new means; corroborating facts have also been received.

Contributions of an original nature concern the fact that for the first time in our country an extended study of the frequency of bone fractures in children and adolescents is carried out. For the first time in our country, data from a study of body composition / distribution in this age group are offered with two methods - DXA and body-impedance. For the first time, the relationship between anthropometric indicators, body composition, bone parameters and metabolic determinants is also studied. Concerning the place of the Contributions section, it would be more appropriate to have them at the end of the text rather than before the bibliography.

8. Evaluation of publications on the dissertation work

The PhD student has submitted 2 full-text publications related to the scientific work. One of them is overview. In both, Dr. Boyadzhiev is the first author, and in the original - and the only one. 3 participations in scientific forums abroad in the form of posters are also presented.

The PhD student has also presented 1 participation in a clinical study on the topic of osteogenesis imperfecta as the main researcher for the country.

9. Personal participation of the doctoral student

The presented dissertation work was created with the personal participation of the doctoral student, and the results and contributions are entirely a consequence of the personal work.

10. Abstract

The abstract covers 100 pages and in terms of content and quality meets the requirements of the relevant regulations. It summarizes in sufficient detail, the main results achieved in the dissertation.

11. Critical remarks and recommendations

Critical remarks and recommendations - it would be beneficial for children with fractures from the epidemiological part to be followed up and, if necessary, additionally examined (for example, for osteogenesis imperfecta). The clinical part is quite small in number and worth expanding in the future. With the expansion of scientific developments, it is also possible to prepare a monograph on this specific problem for children's bone health.

CONCLUSION

The dissertation contains scientific, scientific-applied and applied results, which represent an original contribution to science and meet the requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria (ZRASRB), the Regulations for the Implementation of ZRASRB and the relevant Regulations of the Medical University - Varna.

The dissertation shows that the doctoral student Dr. Veselin M. Boyadzhiev possesses in-depth theoretical knowledge and professional skills in the scientific specialty of Pediatrics, demonstrating qualities and skills for independent conduct of scientific research in the interdisciplinary field of pediatric endocrinology and rheumatology.

Due to the above, I confidently give my positive assessment of the conducted research, presented by the above-reviewed dissertation work, abstract, achieved results and contributions, and I propose to the honorable scientific jury to award the educational and scientific degree "doctor" to Dr. Veselin Milkov Boyadjiev in a doctoral program in Pediatrics.

October 10, 2024 Reviewer:

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§1, б. „В“ от Регламент (ЕС)
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