



OPINION

from Prof. Dr. Valeriya Ignatova Kaleva, MD
Head of the Pediatric Hematology and Oncology Clinic at the
University Multiprofile Hospital for Active Treatment « St. Marina » – Varna

Medical University of Varna
Department of Pediatrics and Medical Genetics

Subject:

Dissertation aiming the award of the education and qualification degree « Doctor »

Subject of the Dissertation: **« Study on bone mineral density and bone turnover markers among Bulgarian patients with transfusion-dependent β -thalassemia, 18+ years old »**

Domain of the Higher degree education: **7. Healthcare and Sports**

Professional domain: **7.1. Medicine**

Doctoral Programme: **« Hematology and Blood Transfusion », Code: 03.01.39**

Author: Dr. Katya Georgieva Sapunarova,
Assistant at the First Department of Internal Diseases, Hematology Section,
Faculty of Medicine, Medical University of Plovdiv

General presentation of the Procedure

Following a Decision at the Meeting of the Faculty Board of the Medical University of Plovdiv and the Scientific Evaluation Committee, I have been nominated to present an opinion on the dissertation of Dr. Katya Georgieva Sapunarova.

The materials submitted in the form of hard copy and electronic copy meet the requirements laid down in art.115, paragraph 1 of the Rules of procedure on the award of the education and qualification degree « Doctor » at the Medical University of Plovdiv and the Regulations of the

Medical University on the development of the Academic Staff of 06.11.2014 and include all the necessary documents : Dissertation, Summary, List and copies of the scientific publications and communications on the subject of the dissertation, a CV of the candidate in an Europass format.

Data on the procedure

Dr. Katya Georgieva Sapunarova's candidacy was officially approved by an Order of the Rector of the Medical University of Plovdiv № 2260 of 22.10.2018 with a related dissertation on the subject « Study on bone mineral density and bone turnover markers among Bulgarian patients with transfusion-dependent β -thalassemia, 18+ years old ». Her research was presented within the time-frame initially set, giving her the right to officially defend her dissertation by a Decision of the Faculty Board Meeting, Protocol №1 of 15.01.2020.

Relevance of the subject-matter

The dissertation presents the existing problem of thalassemia bone disease. There have been no analyses on the osteopenia-osteoporosis syndrome in Bulgarian patients with β -thalassemia. The angle formed by the interaction of the fundamentals of bone biology and the intimate mechanisms of bone response to injury in cases with thalassemia is also relevant nowadays. The formulated scientific hypothesis implies significant correlations between background characteristics, related to thalassemia, and parameters of altered bone metabolism in the frame of a hypertransfusion and chelation therapy, presupposing the possibility to define predictive constellations of prophylaxis and treatment regimes.

Mastering of the problem

The candidate effectuates a wide Theoretical background review of the contemporary concepts for bone injury in patients with β -thalassemia, analyzing scientific data and formulating clinical concepts.

Characteristics and evaluation of the dissertation

The presented *Dissertation* consists of 192 standard pages with 32 tables and 51 figures. The *Theoretical background review* is presented on 34 pages and gives an interpretation of the problem with low bone mineral density and finally formulates a scientific and clinical hypothesis, an objective and tasks. The Section *Materials and Methods* extends on 10 pages in the form of a

diagnostic case-control study, using methodologies for bone mineral density evaluation, bone formation markers and the relevant statistical approaches. The Section *Findings* is illustrated with tables, figures and statistical interpretation of the findings. In the Section *Argument*, the author's findings are being discussed with reference to publications and hypotheses for future research are being defined. In the Section *Conclusions*, 9 conclusions are formulated, determining clear correlations between parameters, related to thalassemia, and indicators for the disruption of bone metabolism.

Assessment of the added value of the dissertation

The added value is extracted in the form of scientific and clinical aspects, which put an accent on risk stratification, molecular and metabolic regulation profile and viral profile.

Assessment of the reference materials

The list of Reference materials includes 303 sources, 8 of which are written in cyrillic alphabet and 295 in roman alphabet and shows evidence on the contemporaneity of publications and the prestige of the journals.

Assessment of the publications, related to the dissertation

Enclosed to the dissertation, there are 4 full-text publications, 3 of which are referenced in the International Database. In addition to that – 3 scientific communications, two of which at Congresses of the European Hematology Association (EHA).

Personal contribution of the candidate

The individual intellectual and scientific activity of the candidate comprises the formulation of a scientific concept, the structuring and design of the study, the effectuation of the research and analyses, data classification and their statistical treatment.

Summary

The summary comprises 61 pages and summarizes the most significant models, researches and analyses, findings, arguments and messages of the dissertation.

Critical analysis and recommendations

From a structural and analytical point of view, the approach is pragmatic and simplified, but as per the multimodality of the factological material the opportunity for multivariate regression on categorical variables of thalassemia related characteristics, molecular and metabolic, laboratory, viral and other parameters has been missed. To that effect, the

conclusions and the recommendations, emerging from the dissertation, could include evidence and recommendations to validate them in the form of algorithms, prognosis and predictions for the respective clinical solutions.

It is recommended for any future scientific studies to have the scientific hypothesis deployed in the following aspects: (1) creation of multivariate regression models for risk impact assessment in relation to the risk of osteopenia-osteoporosis syndrome in patients with β -thalassemia; (2) identification and definition of the predictive markers for the personalization of the therapeutic control of the osteopenia-osteoporosis syndrome.

Conclusion

The dissertation, presented by Dr. Katya Georgieva Sapunarova on the subject « Study on bone mineral density and bone turnover markers among Bulgarian patients with transfusion-dependent β -thalassemia, 18+ years old», fully complies with the requirements laid down in the Act for the Development of the Academic Staff in the Republic of Bulgaria, the Rules on its application and the Regulations of the Medical University of Plovdiv. The presented materials and findings of the dissertation research fully comply with the requirements, set-up in relation to the Rules of Procedure of the Medical University of Plovdiv on the application of the Act for the Development of the Academic Staff in the Republic of Bulgaria.

Having regard to the subject of the dissertation, which is timely and relevant, its methodological competence, its analytical interpretation and its scientific and practical contributions, I firmly give my positive evaluation and propose by the present to the Scientific Evaluation Committee *to vote in favour* in order to award the education and qualification degree “Doctor” to Dr.Katya Georgieva Sapunarova.

Date: 06.03.2020 r.

Drafter of the Opinion :

Prof. Dr. Valeriya Ignatova Kaleva, MD

