

STATEMENT

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Appointed member of the scientific jury by order of the Rector of MU "Professor P. Stoyanov" - Varna with number P-109-139/05.04.2024

about

Dissertation for the degree of "Doctor" of Medicine

Thesis Topic: "Assessment of oxidative stress and early vascular injury in children and young adults with beta-thalassemia major"

Author of the dissertation: Dr. Kristina Ivaylova Petrova, PhD-student at the Department of Pediatrics, Medical University of Varna

Scientific supervisor: Prof. Dr. Valeriya Ignatova Kaleva, Ph.D. and Assoc. Prof. Dr. Maria Stoyanova Dimova - Mileva, Ph.D.

This statement has been prepared in accordance with the Law for the Development of Academic Staff of the Republic of Bulgaria, the Regulations for the Application of the law and the Regulations for the Conditions and Procedure for the Acquisition of Scientific Degrees and Titles and for the Occupation of Academic Positions at MU-Varna.

1. Brief curriculum vitae and professional development of the candidate

The PhD student graduated in Medicine at MU-Varna in 2013. In 2013 Dr. Petrova started working as a resident at the University Hospital "St. Marina" Varna in the Specialized Pediatric Clinic of Clinical Hematology and Oncology, and since 2018 and at present she is appointed as a physician assistant in the same clinic. In 2019 she acquired a specialty in "Pediatric Clinical Hematology and Oncology", and in 2024 - a specialty in "Pediatrics". Since 2018 she is a full-time assistant professor in the Department of Pediatrics, and since 2020 she is a PhD student in the same department.

Additional qualifications related to the dissertation:

In relation to the need for the development of the present work, Dr. Petrova has completed and obtained a qualification in Doppler sonography and a master class in carotid sonography.

2. Relevance of the problem

Beta-thalassemia is a heterogeneous group of diseases characterized by reduced or absent synthesis of beta-globin chains. In individuals with beta-thalassemia major (BTM), unpaired globin chains and high iron concentrations can promote oxidative damage to red blood cells with correspondingly reduced survival in the bloodstream. Although iron is essential for

metabolic processes, excess iron can lead to the production of free radicals. In patients undergoing blood transfusions, iron overload is closely associated with increased oxidative tissue damage; chelation therapy is used to prevent the deleterious effects of excess iron. As the life expectancy of patients with BTM increases, so does the need for accurate and adequate assessment of the degree of oxidative stress.

In this context, the scientific problem for the development of the doctoral thesis is chosen very appropriately.

3. Structure of the dissertation

The doctoral thesis is written in 102 pages (this number of pages does not include the appendices and the bibliography). The text is properly distributed and balanced. The content includes: introduction - 2 pages, literature review - 32 pages, aim and objectives - 1 page, materials and methods - 7 pages, results and discussion - 50 pages, conclusions, contributions, conclusion - 3 pages.

The introduction presents the problem succinctly and clearly, and highlights the challenges that logically motivated the doctoral student to develop the dissertation.

The literature review is contemporary and comprehensive. It gives a comprehensive characterization of the problem under consideration. Presents focused, concise but comprehensive data on beta-thalassemia, oxidative stress theory, its relationship to endothelial dysfunction, both in general and in the context of BTM.

The theoretical background of the dissertant is evident from the presentation. Dr. Petrova has managed to reflect very accurately the state of the problem in the discussed area. The ease with which processes are explained, which by their very nature are extremely difficult to perceive and clarify, is extremely impressive, which is proof that the author has a deep understanding of the subject.

The aim of the study is precisely formulated. The 10 **tasks** are logically outlined - they are specific and feasible. Solving them enables to achieve the set goal.

Materials and Methods: A total of 78 children and young adults, including 38 patients (18 males and 20 females) with beta-thalassemia major and 40 (20 males and 20 females) healthy controls, were the subjects of the study. The study design was "case-control" in a search ratio of 1:1. Controls were matched for age and sex.

The use of modern methods and appropriate statistical processing of data is a prerequisite for obtaining reliable results.

Results and discussion from our own research are presented in detail and appropriately illustrated with 36 tables and 21 figures. Competent discussion, analysis of results and comparison with available data in the medical literature are found logically and skillfully integrated within the communication of each result of the dissertation tasks developed. Although suboptimal, such a thesis structure is acceptable in terms of the accepted rules for writing a doctoral thesis.

The 10 **conclusions** drawn are specific, correct and follow logically from the results obtained.

I agree with the 9 **contributions** highlighted. I consider three of them of a scientific and practical nature to be of particular importance:

-Calculation of lipid indices is a potential clinical tool for cardiovascular risk assessment in patients with BTM.

-Determination of carotid artery stiffness by echo-tracking is an accessible, non-invasive and useful method of assessing vascular health in children and young adults and can be incorporated into the algorithm for follow-up of patients with BTM.

-Identification of subclinical vascular damage is a potential approach for screening and prevention of cardiovascular complications in patients with BTM.

The bibliography includes 358 sources (21 of them by Bulgarian authors), more than 50% of them have been published in the last 10 years.

The dissertant presented 3 **publications** on the topic of the dissertation, two of them in SCOPUS and WOS refereed journals and two contributions to scientific forums. In all publications and presentations the PhD student is first author.

The abstract consists of 72 pages, meets the expected content and gives a clear idea of the essence of the dissertation.

4. Recommendations:

The layout of the thesis - graphically, stylistically and linguistically deserves an excellent grade. The data presented should find a place in a reputable hematology journal in short order.

5. Conclusion:

The dissertation work of Dr. Kristina Ivaylova Petrova entitled "Assessment of oxidative stress and early vascular damage in children and young adults with beta-thalassemia major" is a well-planned study, dedicated to an interesting and topical scientific problem, meets all the requirements for the award of the degree of Doctor of Medicine.

I confidently urge the esteemed members of the scientific jury to give their **positive assessment** and to award the degree of **doctor** of medicine to Dr. Kristina Ivaylova Petrova.

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