

STATEMENT

by

Assoc. prof. Sonya Vasileva Galcheva, MD, PhD

Pediatrician-pediatric endocrinologist, Associate Professor at the Department of Pediatrics,
Faculty of Medicine, Medical University "Prof. Dr. Paraskev Stoyanov" - Varna

Regarding: the dissertation thesis of Dr. Gergana Mladenova Chausheva, a full-time PhD student in "Clinical Laboratory", organized and conducted at the Dept. of Clinical Laboratory, Faculty of Medicine, Medical University "Prof. Dr. Paraskev Stoyanov" - Varna, for the acquisition of the educational and scientific degree "PhD" in the field of higher education 7. Health care and sports, professional direction 7.1. Medicine and PhD Programme "Clinical Laboratory", with scientific supervisor Associate Professor Yana Dimitrova Bocheva, MD, PhD.

Based on Order No. R-109-5/06.01.2023 of the Rector of Medical University "Prof. Dr. Paraskev Stoyanov" - Varna and by decision of the Scientific Jury based on Protocol No. 1/18.01.2023 I have been appointed to prepare an statement (both in Bulgarian and English) for her dissertation "LABORATORY EVALUATION OF CARDIOVASCULAR RISK IN PEOPLE WITH LONG-TERM TYPE 1 DIABETES - ADIPOKINES, OSTEOPRETERIN, ASYMMETRIC DIMETHYL - ARGININE".

The statement was prepared in accordance with the requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria (LDASRB) and the Regulations for the Development of the Academic Staff at the Medical University "Prof. Dr. Paraskev Stoyanov" - Varna.

The stages of the doctoral studies are respected, there is no change of the initial topic and the supervisor. Dr. Chausheva has submitted all documents and materials according to the requirements of the procedure for acquiring the PhD degree according to the requirements of the the MU - Varna.

Brief biographical and professional data about the candidate

Dr. Gergana Chausheva was born on 01/09/1987. She graduated in 2012 as a Master of Medicine at the Medical University of Varna (Diploma No. 001931/2012). In 2016, she obtained a master's degree in "Health Management" (Diploma No. 004126/2016), and in 2018 in the specialty "Clinical Laboratory" (Diploma No. 3917/2018). In 01.2013 - 04.2013 she worked as a clinical laboratory resident doctor at the Medical Center "St. Anna" EOOD, Varna. From May 2013 until now, she has been working as a doctor in the Central Clinical Laboratory at UMHAT "St. Marina", Varna. From February 2017 until now, she has worked as an assistant prof. at the Department of Clinical Laboratory, at MU - Varna. She quickly acquires the competence to carry out teaching activities and adequate professional skills to carry out her dissertation work. She is fluent in English, French

and Russian languages, she has excellent communication and digital skills. She is a member of the Bulgarian Medical Union and the Bulgarian Clinical Laboratory Society.

Relevance of the topic

Diabetes mellitus is a socially significant disease, with a progressively increasing incidence worldwide. As the life expectancy of diabetic patients increases, so does their cardiovascular risk (CVD), making cardiovascular disease (CVD) a major cause for death in diabetes mellitus. Diagnostic-therapeutic approaches aimed at risk assessment, screening and timely diagnosis, and therapeutic behavior of type 1 diabetes mellitus (T1D)-CVD relationship, as they are insufficient and inappropriately based mainly on observations of patients with type 2 diabetes mellitus (T2D).

The evaluation of CVR through the application of innovative laboratory biomarkers would contribute to the improvement of the diagnostic-treatment and prognostic algorithms, with a subsequent reduction in the frequency of concomitant complications, number of hospitalizations and healthcare costs in each individual patient. In this regard, the scientific research of Dr. Chausheva aims to analyze the informative value of the quantification of asymmetric dimethylarginine (ADMA), osteoprotegerin (OPG), adiponectin (ADNC) and leptin (Lep) in relation to the stratification of CVR against specific assessment scales and hematological changes in patients with long-standing T1D.

These facts and the scarce publications in the world's scientific databases, define the topic of the dissertation work as scientifically relevant and of great importance for clinical practice.

Characteristics, volume and structure of the dissertation work

The dissertation work of Dr. Gergana Chausheva is developed on 175 pages and illustrated with 56 tables and 52 figures. She demonstrated a very good and clear style, freely using highly specialized terminology.

1. **The literature review** (42 pages) is modern, well-structured and presents current epidemiological data on T1D and CVD, provides information on scales used to assess CVR in patients with T1D, examines in details the new classes of laboratory biomarkers (asymmetric dimethylarginine (ADMA), osteoprotegerin (OPG), adiponectin (ADNC) and leptin (Lep)), analyzing the possibility of their validation in CVD assessment in order to improve the screening, diagnosis and prognosis of CVD in patients with long-term T1D. In the review the author did an excellent interpretation of worldwide literature confirming the good theoretical knowledge of the candidate on the dissertation topic and the latest research in the field.

2. **The aim and the tasks** (1 page) of the work are clearly formulated, with 6 main tasks corresponding to the set research aim.

3. **Material and methods** (6 pages). Dr. Chausheva's dissertation work is a part of a long-term and large-scale work on a scientific project, supported by the "Scientific Research" Fund at the Ministry of Education and Science, with participating specialists from various preclinical and clinical units. The study design, the characteristics of the participants (124 patients with T1D and 59 healthy volunteers) and the methods used to fulfill the tasks and scientific aim are presented clearly and

fully competently by the author. The work was carried out entirely according to the rules of the good scientific practice, after obtaining permission from the Committee on Ethics of Scientific Research at the Medical University of Varna.

4. **Own results** (70 pages). In a total of 70 pages, Dr. Chausheva describes in detail and sequentially the implementation of each of the set tasks, leading to the fulfillment of the clearly formulated aim of her scientific work. They are well illustrated with 56 tables and 52 figures, accompanied by an understandable text, and the applied statistical analysis is correctly chosen and performed. A good prognostic value of OPG and Lep is demonstrated for differentiating individuals of both sexes with high CVR, with inferred threshold values that require the implementation of urgent preventive measures. A positive association between Lep, ADNC and OPG levels and the presence of hypochromic, microcytic anemia in patients with long-standing T1D was demonstrated, the risk of the latter being greater among men.

5. **Discussion** (31 pages). In this section, Dr. Gergana Chausheva makes an in-depth analysis of her results, comparing them with those of other national and foreign scientific teams. All this shows the good level of preparation of the PhD candidate, who demonstrates excellent knowledge of national and worldwide literature on the problem. There is an openness and admission of some of the study limitations, which I personally admire.

6. **Conclusions and contributions** (3 pages). Consistently, clearly and in accordance with the obtained results, 12 conclusions are formulated, which follow the tasks set in the dissertation work. 10 contributions of scientific and practical importance have been formulated, 4 of which are original for the country.

7. **Bibliography** (14 pages). The list of cited literature includes 307 sources - 14 in Cyrillic and 293 in Latin, and 72% are from the last 10 years.

8. **Publications and messages on the subject** (1 page). A list of 2 full-text publications and 4 participations in international conferences is presented. In all publications, Dr. Chausheva is the first author. The scientific activity of the student is in accordance with the normative requirements.

9. **The abstract** (108 pages) has been developed and structured according to the requirements, and its content fully corresponds to the dissertation work.

Critical notes

The work is original, with an excellent research design and clearly set goals and objectives, as a result of which the conclusions are drawn and the essential contributions of the scientific work are determined. It is important to note that the realization of Dr. Gergana Chausheva's dissertation work is part of a larger scientific project "Cardiovascular and metabolic risk associated with visceral adipose tissue in patients with type 1 diabetes mellitus", supported from the "Scientific Research" Fund at the MES. All this shows the responsible attitude of the PhD student, which is an excellent assessment of the team and the work of and of her supervisor.

CONCLUSION

The dissertation submitted for review is the author's own work, which is characterized by originality, relevance, thoroughness and an important scientific-applied nature. Dr. Gergana Chausheva is an excellent specialist who put a lot of personal work, patience and persistence into her research work. The development fully complies with the Law on the Development of the Academic Staff in the Republic of Bulgaria, the Regulations for its implementation and the Regulations for the Development of the Academic Staff at the University of Medicine - Varna.

All this gives me reason to give my **positive opinion** with conviction and to recommend to the respected Scientific Jury to award the educational and scientific degree "Doctor" to Dr. Gergana Mladenova Chausheva.

07.02.2023

Varna, Bulgaria


.....
Assoc. prof. Sonya Galcheva, MD, PhD