

To the Chairman of the Scientific Jury  
appointed by Order № P-109-  
5/06.01.2023 of the Rector of Prof. Dr.  
"Paraskev Stoyanov" Medical University  
of Varna

## STANDPOINT

**Prepared by:** Assoc. Prof. Marianka Genova Petrova-Yanachkova, MD, PhD, Member of the Scientific Jury

**Scientific specialty:** Clinical Laboratory, Faculty of Medicine, Medical University, Sofia

Department of Clinical Laboratory, Faculty of Medicine, Medical University, Sofia

**Contact:** Postal address: 1, Sv. G. Sofiyski Blvd., 1431 Sofia

Email: mariana8sofia@yahoo.com

Phone: 02/ 9230-927; 0888405382

**Regarding:** Defense of a dissertation and procedure for acquiring the educational and scientific degree "DOCTOR"

**The professional field:** 7. Health and Sports

**Professional direction:** 7.1 Medicine

**Doctoral program:** Clinical laboratory

**PhD Candidate:** Dr. Gergana Mladenova Chausheva

Department of Clinical laboratory, Medical Faculty, Medical University Prof. Dr. "Paraskev Stoyanov" of Varna

A thesis on the topic: **LABORATORY CARDIOVASCULAR RISK ASSESSMENT IN INDIVIDUALS WITH LONG-STANDING TYPE I DIABETES MELLITUS–ADIPOKINES, OSTEOPROTEGERIN, ASYMMETRIC DIMETHYL-ARGININE**

**Scientific supervisor:** Prof. Dr. Yana Dimitrova Bocheva, PhD

**Department of Clinical laboratory, Medical Faculty, Medical University "Prof. Dr. Paraskev Stoyanov" of Varna**

Appointed a member of the scientific jury according to the decision of the Faculty Council of Medical University, Varna and protocol №78/19.12.2022. At the first meeting of the Scientific Jury, held on 17.01.2023, I was chosen to prepare an opinion on the procedure for acquiring the educational and scientific degree "DOCTOR".

The given materials meet the requirements of the Law for Development of the academic science of the Republic of Bulgaria and the criteria for accrediting scientific entitlements at the Medical University "Prof. Dr. Paraskev Stoyanov" of Varna

**Biographical data and professional development of the doctoral student**

Dr. Gergana Mladenova Chausheva was born in Varna, where she graduated high school in foreign language high school "Frederik Julio-Curie". She had her master's degree in medicine at the Medical University "Prof. Dr. Paraskev Stoyanov" of Varna in 2012, diploma No. 001931. In 2013 she started working as specialist "Clinical laboratory" in Medical Centre "St. Anna", Varna. Since May 2013 she has been working in the Central clinical laboratory at the University hospital "St. Marina", Varna. In 2017 she became an Assistant Prof. in the department of Clinical laboratory at Medical University "Prof. Dr. P. Stoyanova" of Varna, where she actively participated in the teaching process to students. In 2018 she became a specialist in Clinical laboratory, diploma No. 3917. Dr Chausheva has graduated also "Healthcare management" in 2016, diploma No.004126. She is a full time doctorant according to mandate № P-109-515/05.11.20 by the Rector of the Medical University "Prof. Dr. P. Stoyanov" of Varna Prof. Dr. Valentin Ignatov.

Dr Chausheva is a member the Bulgarian Society of Clinical Laboratory and the Bulgarian Medical Union.

### **The relevance of the thesis**

Diabetes mellitus is a chronic disease with great social impact, its prevalence rises not only worldwide, but also in Bulgaria. The diagnosis "Diabetes mellitus Type 1" (DM T1) is associated with lots of challenges: the need for regular checks of the blood sugar levels and correction of the insulin-doses with the aim of preventing acute and long-term adverse outcomes. The most important of them are the cardiovascular complications (CVC). It is a well-known fact, that patients with DM T1 have a higher risk for CVC, especially the ones diagnosed with this disease in childhood. These patients have 8-fold higher risk of hospital acceptance in a young adult age (30-44years). An important fact about this phenomenon is also that adverse complications are more common with female rather than male patients. The prevalence of CVC in men and women with DM T1 is equally dispersed, but it is higher in the common male population. The risk stratification and screening strategies for evaluation the CVC in patients with DM T1 are still not well known. That is why the introduction of different laboratory biomarkers and combinations of these could optimize the diagnostic pathway, the prognosis and the therapeutical options for the patients. The scarce literature on the topic, as well as the relevance of the problem, show us the importance and the possible effect of this thesis for the clinical practice.

### **Structure and characteristics of the thesis**

The dissertation is structured according to the requirements, written in a formal scientific style, logically constructed, which makes it easy to read and understand. It is 175 pages long; there are 56 tables and 52 figures. All the necessary elements such as heading, content, abbreviations, introduction, summary of papers, aim of the thesis, methods and materials, results, discussion, conclusion. There are 12 conclusions and future prospects, differentiated according to originality: 4, prospects with theoretical and scientific character: 6. The bibliography is structured according to the requirements, there are 307 sources, 14 of them in Cyrillic, 293 in Latin. The majority of the papers were published in the last 10 years, there are cited authors from the recent 2-3 years; the authors are arranged alphabetically, which makes me happy.

### **Evaluation of the structure of the dissertation**

Summary of papers: well structured, shows the ability of the doctorant to work with scientific literature. It is printed on 41 pages. A thorough and detailed analysis and description of the laboratory indicators like ADMA, OPG, ADNC and Lep was made. Each one of them is described and discussed upon its structure, synthesis, biological role in the organism and its role in

pathophysiological mechanisms in the development of CVC and its clinical importance. It makes very good impression the detailed description and summary of the modern analytical methods to measure this indicator with the reference range, presented very well in tables.

Deriving from the summary of papers and the conclusions, Dr. Gergana Chausheva describes two aims of this dissertation: to analyze the prognostic value of ADMA, OPG, ADNC and Lep in comparison to specific tools that evaluate CVC: ST1RE and ESC from 2019 and the same indicators in comparison to hematologic indicators in patients with DM T1 diagnosed for a long time. From these aims the six tasks of this scientific work rightfully derive.

### **Materials and methods**

They are accurately chosen and related to the aim and the tasks of the dissertation. In the study the control group is consisted of 59 people and 124 patients, female and male altogether, diagnosed with DM T1 more than 15 years.

This dissertation is part of the scientific project "Cardiovascular and metabolic risk, associated with visceral fat tissue in patients with DM T1", supported by the foundation "Scientific studies" by the Ministry of education and culture (contract DN13/3, 14.12.2007). The material used is enough to produce statistically significant results. The indicators ADMA, OPG, ADNC and Lep were measured by ELISA methods, whose characteristics are profoundly shown in table in the study. The calculators for evaluation of clinical indicators for CVC are described, too.

The results are analyzed via accurately chosen and thoroughly described 9 statistical methods. SPSS 19 was used as statistical programme.

### **Results and discussion**

The results of the study-tasks are presented clearly with tables and figures, such as histograms, graphs, ROC curves with very good quality, which visualize very clearly the thesis of the dissertation. Moreover, the dissertant interprets the statistical results very well, which shows her knowledge of the use of the different statistical methods and how to handle them.

The discussion shows its own results compared to the literature data, if any data was found available. When information was missing or the correlation was not clear, the dissertant gave logic explanations. The discussion shows, that Dr. Chausheva is capable of using the literature data and concretizing data specifically correlating to the results from her study.

The discussion of the studied indicators shows:

-ADMA indicates tendency towards lower values with aging and the increasing longevity of the DM T1 disease. It correlates well with albuminuria in patients with DM T1 without being able to differentiate patients with low and moderate risk of CVC and patients with high risk of CVC

-OPG correlates positively with longevity of the Diabetes mellitus-diagnosis, the albuminuria and risk factors for CVC: Risk Factor 3 and ST1RE in patients with DM T1

-ADNC presents correlation with the longevity of the DM-diagnosis, significant negative correlation with BMI, stronger in men than in women with DM T1, no correlation with the factors of CVC: STRE, ESC from 2019, Risk Factor 3 and other important markers of Diabetes mellitus (DM) like Albu, CRP, and HbA1C

-Lep shows very good statistically significant correlation with BMI in both sexes in patients with DM T1 and association with men's age. It is associated with clinical risk factors of CVC: Risk Factor 3, ESC from 2019, ST1RE, the albuminuria in both sexes and CRP in women with DM T1

The investigated indicators had a cut-off value for patients with DM T1 and another cut-off value for CVC risk in patients with DM T1, diagnosed long time ago.

To complete the tasks of this study, connections between the hematological indicators were investigated. The tendencies towards leukocytosis, higher platelet-count and thrombocyte indices in patient with long-term DM T1, as well as correlations with other hematomorphological factors.

After the discussion and the conclusion of the results, 12 implications and 10 inputs were derived in accordance with the tasks and the results. The future inputs were divided in theoretical and practical.

### **Publication activity**

In the end of this dissertation there is a list of publications and enrolments in scientific forums, associated with this work, in the autoreferat and it is in accordance with the requirements on the terms and conditions for acquiring scientific degrees and occupying academic positions by the Medical University "Prof. Dr. Paraskev Stoyanov" of Varna.

**Abstract:** meets the regulations, 108 pages long, consisting of major parts of this work, tables, figures, ROC curves. The content gives a detailed idea about the whole dissertation.

**Critical note:** When preparing the dissertation, the full stop "." at the end of the sentence must be typed after the cited source in brackets, not before it.

**In conclusion:** The presented scientific work by Dr. Gergana Chausheva is full, relevant, detailed, well-structured and completes the clearly defined tasks, with important conclusions and contributions to the contemporary science and of great practical orientation, that can be introduced in the daily practice. The current dissertation once again shows the important role of laboratory tests in the diagnostic process, not only as a supplement to the clinician's work, but also as an opportunity for prevention and early targeting of the problem before its clinical manifestation

All the above gives me a reason to recommend to the esteemed members of the Scientific jury and according to the requirements of the Law on the development of the academic staff in the Republic of Bulgaria, the Rules for Implementation of the Law on the development of the academic staff in the Republic of Bulgaria and the Regulations on the terms and conditions for obtaining scientific degrees and holding academic positions at Medical University "Prof. Dr. Paraskev Stoyanov" of Varna to award Dr. Gergana Mladenova Chausheva degree of "Doctor" of Education and Science in the scientific specialty Clinical Laboratory in the professional field 7.1 Medicine in Higher Education 7. Health and Sports.

Sofia,

03.02.2023

  
.....  
Assoc. Prof. Dr. Marianka Genova Petrova-Yanachkova, PhD