

To the Chairman of the Scientific Jury,  
Assigned by Order  
№ P-109-160/14.03.2025  
of the Rector of Medical University - Varna

#### **BRIEF REVIEW**

by **Assoc. prof. Nevena Yankova Chakarova, MD, PhD**

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University Hospital of Endocrinology "Acad. Ivan Pentchev", Division of Diabetology

on the doctoral thesis of **Zhaneta Atanasova Yaneva, MD**,  
doctoral fellow at the Second department of Internal diseases,  
ES "Endocrinology", Faculty of Medicine, Medical University of Varna,  
with academic supervisor **Assoc. prof. Mila Boyadzhieva, MD, PhD**,

on the topic: *„Glycemia in acute ischaemic stroke - prognostic significance and association with metabolic and inflammatory markers”,*

for educational and scientific degree *Doctor of Philosophy*, area of higher education code 7.  
*Health care and sports*, professional division code 7.1 *Medicine*, doctoral program *Endocrinology*

I have been elected as an external member of the scientific jury by order № P-109-160/14.03.2025 of the Rector of Medical University of Varna. In compliance with the decision of the first meeting of the jury - Protocol №1/25.03.25, I have been appointed to provide a brief review on the abovementioned doctoral thesis.

I declare full registration in NACID and no conflicts of interest.

The review is based on the presented complete set of documents in compliance with the Law on the Development of the Academic Staff in the Republic of Bulgaria and the regulations of Medical University of Varna.

#### **1. Relevance of the topic**

The topic of the doctoral thesis is of exceptional present interest and great practical importance. Currently, there is no consensus statement and clear clinical guidance for the assessment of glycemic status and therapeutic targets in patients in intensive care units including those with acute stroke. Therefore each research in the field is topical and relevant.

With the introduction of the new therapeutic agents for the treatment of type 2 diabetes and their organprotective properties, the macrovascular disease has been placed in the focus of the scientific interest, laying the stress on the opportunities for prevention and risk reduction thus

underscoring the question for the assessment of glycemia, its management and prognostic value in the setting of already present acute vascular event.

The present study so far is the first of the kind for a Bulgarian population which adds to the value and the relevance of the doctoral thesis.

## **2. Structure**

The doctoral thesis comprises 143 standard pages and is divided into the following sections - Literature review 33 pages., Aim and tasks - 1 pages., Material and methods 5 pages., Results - 57 pages., Discussion and conclusions - 20 pages., Contributions 1 pages., References - 13 pages with 285 sources, 9 of which written in Cyrillic and 276 - in Latin, 77 (27%) published in the last 5 years and 142 (49.8%) - in the last 10 years.

### **2.1 Literature review**

The literature review is comprehensive, well-structured and logically built. The presentation is concise and to the point, with critical analysis of the present data and without unnecessary information. The presentation outlines the unsolved questions in the field and demonstrates the in-depth knowledge of the doctoral student. From endocrinological point of view all parameters for the assessment of glycemic control - both classical and new ones including glucose variability as well as the HbA1c-based glycemic indices for the assessment of stress hyperglycemia, are discussed exhaustively. The part of the review related to the description of stroke as well as the theoretical background from the field of neurology is presented very well demonstrating the solid knowledge of the doctoral student in general medicine. A separate part of the review is dedicated to some inflammatory markers as potential diagnostic and prognostic markers in acute stroke. An innovative part of the research is represented by progranulin which is included together with the classical inflammatory markers. A substantial part of the cited publications is from the last 5 years - about 1/3, the most recently published meta-analyses and publications of Bulgarian authors on the topic are also included in the review.

**2.2 The aim and the tasks** of the study are clearly stated and the tasks correspond to the predefined aim.

**2.3 The material and methods** are presented comprehensively, correspond and are relevant to the listed tasks.

**2.4 The results** are presented in detail. The section is well-structured and sufficiently visualized in tables and figures easily understandable by the reader. The description of the results is clear and correct.

Of both theoretical and practical importance are the results for the group with stress hyperglycemia as they outline this subgroup of patients as the one at the highest risk in acute stroke. The advantage of the glycated hemoglobin based indices over the rest of the glycemic parameters for the diagnosis and risk stratification of the patients with stroke is clearly shown.

Of great importance for the clinical practice is the identification of feasible parameters for the assessment of the severity and prognosis of stroke such as the leucogram, cortisol levels, CRP and HbA1c-based indices.

The obtained results for progranulin are of contributive value as they outline its discriminative and potential prognostic value in acute stroke.

I find particularly interesting the results for the total and LDL-cholesterol and their relation to the prognosis of stroke.

**2.5 The discussion section** is well structured and follows the concise style of the doctoral student with no irrelevant information. The results are analyzed and discussed correctly. The limitations of the study that can potentially influence the results are clearly pointed out.

The **conclusions** are stated in a clear and moderate manner and are derived strictly from the obtained results.

**2.6 The contributions** are divided into such of original or confirmatory character and are listed clearly and correctly.

I find particularly valuable and important for the clinical practice the presented analyses for the prevalence of stress hyperglycemia in acute stroke, the different methods for its assessment and the established superiority of the HbA1c-based indices and the relation of stress hyperglycemia to the severity and prognosis of stroke.

The study is the first of the kind for a Bulgarian population that makes it a valuable contribution on national basis while the relevance of the research and the additional assessments of cortisol and progranulin are important contributions on international basis.

### **3. Publications**

In relation to the doctoral thesis the doctoral fellow has published 4 papers in national journals, one of which is indexed in international scientific data bases /Scripta Scientifica Medica/. Dr. Yaneva is the first author of all 4 papers that guarantees her leading role in the research and in the publication process. Parts of the doctoral thesis are presented at 4 scientific meetings - 3 national and 1 world congress, and Dr. Yaneva is the first author of all presentations.

Dr. Yaneva has participated in 1 scientific project in relation to the topic of the doctoral thesis funded by Medical University of Varna.

### **4. Personal contribution**

The personal contribution of the doctoral student in the scientific research and the dissemination of the obtained results is self-evident from the presented set of documents.

**5. The summary** of the doctoral thesis reflects the principle results of the study and is written in compliance with the regulations of Medical University of Varna.

### **6. Remarks and recommendations**

**I have no critical or basic remarks on the presented doctoral thesis.**

I would like to recommend the following for the present and future research:



- The very high mean value of CRP in the group with stress hyperglycemia is noticeable - I suggest a reanalysis of the data set with exclusion of the extreme values of probable infectious origin
- Increase of the number of the publications in relation to the doctoral thesis – I believe that the presented research is of high value and quality and has the full potential for dissemination in international journals with impact factor
- Application and participation in new scientific projects that could provide opportunities for funding for continuation of the research with the implementation of the continuous glucose monitoring as a tool for the assessment of glycemic control and glucose variability

## CONCLUSION

In conclusion I state that the presented doctoral thesis is relevant, the design of the study and the applied methods are appropriate and precise, the obtained results are discussed and summarized correctly. The presented doctoral thesis reveals the solid theoretical background of the doctoral student including areas of medicine beyond the scope of the particular speciality as well as her capability of performing independently scientific research in accordance with the highest standard. I would like to emphasise as a great advantage of the thesis its marked clinical focus and clear relevance of the obtained results and conclusions to the clinical practice.

The doctoral thesis is in full compliance with the Law on the Development of the Academic Staff in the Republic of Bulgaria and the regulations of Medical University of Varna.

**Based on the above stated I declare my positive review and recommendation to the other members of the scientific jury to award the educational and scientific degree *Doctor of Philosophy* to Zhaneta Atanasova Yaneva, MD.**

19.04.2025  
Sofia

Respectfully  
Assoc. prof. Nevena Chakarova, MD, PhD

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