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STATEMENT

by Assoc. Prof. Darina Kirilova Georgieva-Hristova, MD, PhD

Associate Professor at the Department of Neurology and Neurosciences, Faculty of Medicine Medical University "Prof. Dr. Paraskev Stoyanov" - Varna

Member of the Scientific Jury, appointed by Order No. R-109-160/14.03.2025 of the Rector of the Medical University "Prof. Dr. Paraskev Stoyanov" - Varna

Regarding the Dissertation Thesis

of Dr. Zhaneta Atanasova Yaneva

on the topic: "Glycemia in acute ischemic stroke - prognostic significance and relationship with metabolic and inflammatory markers."

for awarding the educational and scientific degree Doctor in the field of higher education
7. Health and sports, professional direction 7.1 Medicine and the doctoral program
Endocrinology

Scientific supervisor: Assoc. Prof. Mila Bogdanova Boyadzhieva, MD, PhD

Based on order No. R-109-160/14.03.2025 of the Rector of the Medical University "Prof. Dr. Paraskev Stoyanov" - Varna, based on a decision of the Faculty Council of the Faculty of Medicine (Protocol No. 36/10.03.2025) I have been elected as an internal member of the Scientific Jury evaluating the dissertation work of Dr. Zhaneta Atanasova Yaneva on the topic "Glycemia in acute ischemic stroke - prognostic significance and relationship with metabolic and inflammatory markers".

According to a decision from the first meeting of the scientific jury, I have been assigned to prepare an opinion. The presented set of materials on the procedure for awarding the procedural requirements for obtaining the academic degree Doctor is complete, available in electronic and paper format and is in accordance with the requirements of the Low on the Development of Academic Staff in the Republic of Bulgaria and the Regulations on the Development of Academic Staff of the Medical University - Varna.

Brief biographical data

Dr. Zhaneta Atanasova Yaneva obtained the educational qualification degree of a Master's in the specialty of Medicine at the Medical University of Varna in 2013, an excellent student of her class. In 2016, she obtained a master's degree in Health Management, and then in 2021, earned the specialty "Endocrinology and Metabolic Diseases".

Dr. Zhaneta Yaneva's professional path started in 2014, as a physician at the "Clinic of Endocrinology and Metabolic Diseases" at the University Hospital "St. Marina" in Varna. In 2016, she began her academic career, as a part-time assistant within "Department of Internal Medicine" at the Medical University - Varna, and since 2017 she is an assistant at the Second Department of Internal Medicine, Department of Endocrinology at the Medical University of Varna, conducting treatment, teaching and research activities. She is a teacher of medical students (Bulgarian and English-language training) and specializing doctors. Her main interests are in the field of diabetes mellitus.

Dr. Yaneva annually participates in the annual National Congress of Endocrinology, as well as in a number of national and international scientific forums, including as a lecturer. She is a coauthor of a textbook on Internal Medicine for healthcare professionals. The continuing education courses conducted further contribute to her development as an excellent specialist. In 2023, she completed an internship in rare endocrine diseases at the University Hospital in Munich, Germany.

Dr. Yaneva is a member of the Bulgarian Society of Endocrinology (BSE), Bulgarian Medical Union (BLS She is fluent in English, German and Russian, using them in her professional activities.

Relevance and significance of the topic

Ischemic strokes are a leading cause of mortality and long-term disability worldwide. Bulgaria is placed second in the world rankings in stroke morbidity and mortality.

Glycemic control is of utmost importance for patients with acute ischemic stroke, as maintaining glucose levels within certain limits is of particular importance, both for the course of the stroke and for the clinical and functional outcome. This makes the topic of the dissertation relevant and of exceptional importance in daily clinical practice.

Acute ischemic stroke, as an acute disease that puts the body in a state of stress, is often accompanied by stress hyperglycemia.

Blood glucose is a modifiable risk factor for stroke that can be therapeutically influenced. This requires understanding the impact of abnormal glucose levels on the course and prognosis of acute cerebrovascular accident.

The discovery of laboratory parameters associated with blood glucose, as well as the identification of various biomarkers with predictive value, would be useful in determining the patient's risk profile, as well as prognostic factors for the course and outcome of acute cerebrovascular accidents in assessing the risk of death, as well as in making decisions about therapeutic behavior.

It is the indispensability for further studies on the role of glycemia in acute ischemic stroke that is the focus of the present study.

Structure of the dissertation

The dissertation contains 137 standard pages and is illustrated with 38 tables, 28 figures and 4 diagrams. The content is presented correctly and in detail. The most frequently used abbreviations are listed. The bibliography contains 285 titles, of which 9 are in Cyrillic and 276 in Latin. The individual chapters and subchapters are properly formatted, which provides clarity and readability of the dissertation.

Literature review

The literature reviews demonstrates a very thorough knowledge of the sources and the extraction of in-depth information from them. It is purposefully constructed, emphasizing relevant aspects of the main topic. Historical data, prevalence, clinical significance, pathogenesis and mechanism of action of stress hyperglycemia are presented in detail.

In the next stage, the author emphasizes the role and damaging mechanisms of stress hyperglycemia, as well as glycemic variability in acute ischemic stroke. The complex interaction between the central nervous system and the peripheral immune system, namely the activation of a complex neuroinflammatory response, following acute cerebral ischemia, is examined. In this aspect, the role of some metabolic and inflammatory markers with potential significance in acute ischemic stroke is examined.

The aspects covered in the literature review represent an adequate justification for the purpose and objectives and argue the motivation for developing the dissertation topic.

Goal and objectives

The goal is formulated precisely, namely: "To search for a relationship between the level of glycemia and the outcome in patients with AMI, as well as an association with metabolic and inflammatory markers."

To achieve this goal, five clearly defined tasks have been set.

Materials and Methods

The study was conducted in two stages.

The first stage started with a retrospective study of a cohort of a total of 555 patients with acute MI aged 25 to 98 years with a similar proportion of men and women, hospitalized in the Second Clinic for Nervous Diseases with intensive care unit for neurological diseases and acute stroke treatment unit of the University Hospital "St. Marina" - Varna due to acute MI for the period May 2016 - April 2017. The participants were selected according to certain inclusion and exclusion criteria.

In the second stage, a retrospective cohort study was conducted of a total of 114 patients with acute ischemic stroke aged 43 to 93 years, with a comparable proportion of men and women, hospitalized for acute ischemic stroke in the Second Clinic for Nervous Diseases with intensive care unit for neurological diseases and acute stroke treatment unit of the University Hospital "St.

Marina"-Varna for the period June 2021-May 2023. Patients were selected in the first 24 hours of hospitalization according to relevant inclusion and exclusion criteria.

Due to the selection of patients during a period including the Covid-19 pandemic, a rapid antigen test for Covid-19 was performed on all patients. All patients included in the study tested negative.

The study is complex, representative and comprehensive. Modern, diverse and appropriate statistical methods have been applied, allowing for analysis of the researched indicators, which allows for drawing clear and specific conclusions.

Results

The results of the study are precise and convincing, illustrated comprehensively with figures and tables. Subgroup comparative analyses of the studied indicators with the severity of acute ischemic stroke, as well as with the functional outcome of the disease, were made. The results are divided into two parts - for the first and second stages of the study, respectively.

Of particular interest are the observations regarding HbA1c-based glycemic indices, all of which showed significant differences between groups. As markers of acute stress hyperglycemia, similar to the severity of acute ischemic stroke on admission, they demonstrated significantly higher levels in the stress hyperglycemia group compared to the other groups.

Of interest is the serum marker progranulin, which, although mainly associated with neurodegenerative diseases, could also be used to assess the severity and prognosis of acute stroke.

Discussion

This section demonstrates Dr. Yaneva's excellent literature awareness and analytical thinking. The discussion of the results presents an in-depth analysis between her own results and the data in the literature.

The widespread prevalence of glycemic disorders in patients with acute ischemic stroke and the related need to clarify the glycemic status of these patients are discussed. In this aspect, factors associated with glycemic status and their prognostic significance in patients with acute ischemic stroke are considered in detail. It is comprehensive discuss that stroke severity also correlates with stress response indicators - serum cortisol levels, as well as HbA1c-based glycemic indices.

Conclusions

The conclusions are formulated in 9 points, reflecting the significant results obtained by Dr. Yaneva. The presented conclusions accurately and completely correspond to the obtained results.

As a neurologist, I believe that the findings proving that both stressful and persistent hyperglycemia, high cortisol levels, and high neutrophil/lymphocyte ratios are associated with poor functional outcome and an increased risk of fatal outcome in patients with acute ischemic stroke are of utmost importance.

Contributions

The above contributions are original and confirmatory in nature.

The prevalence of stress hyperglycemia in patients with acute ischemic stroke has been studied for the first time in the country. In this aspect, Dr. Yaneva's work is of exceptional contribution to clinical practice, both for neurologists and endocrinologists, and for the entire medical community.

For me, as a neurologist who in my daily practice mainly encounters patients with cerebrovascular diseases, the confirmation that stress hyperglycemia is observed in patients with more severe acute ischemic stroke and is associated with a worse functional outcome, as well as higher mortality, is of great importance.

The established association between glycemic disorders, some metabolic and inflammatory markers with the outcome of acute ischemic stroke supports timely decision-making for therapeutic behavior.

Sources used

The bibliographic reference includes 285 titles, of which 9 are in Cyrillic and 276 in Latin.

Publications and scientific events related to the dissertation:

A list of publications and participation in scientific forums and projects related to the dissertation is presented.

Dr. Zhaneta Yaneva is the first author in four full-text publications. She has four participations in national and international scientific forums.

In connection with the dissertation work, she participated in a project on the topic "Glycemia in acute ischemic stroke - prognostic significance and relationship with metabolic and inflammatory markers" - funded by the Science Fund at Medical University of Varna. The scientific study was approved for conduct by the Research Ethics Committee at MU-Varna

The abstract of the dissertation is available in electronic and paper format. It includes a total of 78 pages and is illustrated with 18 tables and 28 figures. The abstract is structured according to the requirements and its content corresponds to the dissertation.

Conclusion

In terms of structure, volume and content, the presented dissertation meets all the requirements of the Act on the Development of the Academic Staff in the Republic of Bulgaria (ADSRB), the Regulations for the Implementation of the ADSRB and the relevant Regulations of MU-Varna.

It is an original work of the dissertation candidate, demonstrating in-depth theoretical training, professional skills and the ability to conduct scientific research.

Based on the submitted dissertation, I believe that Dr. Yaneva has complex and comprehensively developed her scientific thesis, concerning a current interdisciplinary aspect related to glycemic disorders in patients with acute ischemic stroke.

An important aspect in the neuro-endocrinological field is examined, which has not yet been developed and analyzed in detail and in depth in Bulgaria. As a neurologist, I believe that the dissertation work of Dr. Zhaneta Atanasova Yaneva is of exceptional significance for neurological practice in the treatment of patients with acute ischemic stroke.

Given all of the above, I confidently give my positive assessment and propose to the esteemed members of the Scientific Jury to give a positive assessment to the dissertation work of Dr. Janeta Atanasova Yaneva for the acquisition of the educational and scientific degree Doctor.

		Заличено на основание чл. 5,	
		§1, б. "В" от Регламент (ЕС)	
17.04.2025	Prepared by	2016/679	
			Ι.

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