OPINION

by assoc. prof. Kosta Dimitrov Kostov, MD, PhD

Medical Institute - Ministry of Internal Affairs, Sofia

ON the dissertation of Vladina Miroslavova Dimitrova-Kirilova, MD, entitled "Occupational predisposition in asymptomatic stroke" with academic supervisor Prof. Veselinka Dimitrova Nestorova, MD, and awarding the educational and scientific degree "Doctor" of Medicine in area of higher education 7. Healthcare and Sport, professional field 7.1. Medicine, doctoral program "Occupational diseases" at Medical University "Prof. Paraskev Stoyanov" – Varna.

I was appointed member of the Academic Jury on the dissertation of Vladina Dimitrova-Kirilova, MD with MU-Varna Rector's Order № P-109-37/25.01.2023 and Protocol № 1/26.01.2023 of the first session of the Academic Jury.

Vladina Miroslavova Dimitrova-Kirilova, MD was born in 1988 in Dobrich where she completed her secondary education in 2007. In 2013 she graduated cum laude the "Medicine" MA programme at MU-Varna. In 2021 she earned a specialty in "Neurology".

Dr. Dimitrova began her career in October 2013 as a physician at CEMS-Varna, Dolni Chiflik branch, where she worked until May 2015. In June 2015 she began her post-graduate studies at the Second Neurology Clinic at University Hospital St. Marina – Varna. In 2017, she won a competition for assistant professor at the Training sector of Occupational Diseases, setting her academic career in motion, and in 2018, began her full-time doctoral studies in "Occupational diseases" at the Training sector of Occupational Diseases, Department of Optometry and Occupational Diseases, MU-Varna, in the 7.1. Medicine professional field.
Dr. Vladina Dimitrova teaches "Occupational diseases" to Bulgarian- and English-speaking medical students at MU-Varna, as well as "Neurological diseases" to students studying Kinesiotherapy and Speech Therapy. She has participated in a number of qualifying thematic post-graduate courses: Regulation on the education of doctoral students; Methodology of scientific research; Research ethics; Statistical methods for data processing and presentation; Communication techniques and presentation skills among others. Dr. Dimitrova is a member of the Bulgarian medical association, the Bulgarian Society of Neurology and the European Stroke Organisation.

The dissertation presented to me is in accordance with the terms and conditions outlined in the ADASRB (Act for the Development of the Academic Staff in the Republic of Bulgaria), RAADASRB (Regulations for the Application of the Act for the Development of the Academic Staff in the Republic of Bulgaria) and the relevant Regulations at MU-Varna. Dr. Dimitrova's dissertation is 122 pages long and contains 21 figures and 17 tables. It consists of list of contents (2 pages), abbreviations (1 page), introduction (1 page), literature review (41 pages), purpose and goals (1 page), working hypotheses (1 page), materials and methods (2 pages), results (23 pages), discussion (8 pages), opinion (1 page), conclusions (1 page), contributions (1 page), bibliography (25 pages), publications and participations in scientific forums related to the dissertation (1 page)

and appendices (7 pages). The structure of the work is in compliance with the regulatory requirements described in the Regulation for the development of the Academic Staff at MU-Varna.

The topic of the dissertation is quite relevant as it is related to a socially significant disease – cerebrovascular disease, one of the leading causes of disability and death, including in working age adults. Recent advancements in neuroimaging methods and magnetic resonance imaging have enabled the discovery of some forms of the disease which do not manifest clinically, the so-called asymptomatic, or "silent", cerebrovascular disease. Dr. Dimitrova has focused her research specifically on the risk factors for the silent forms of the disease. Occupational risk factors are an unavoidable part of a worker's life, having a continual effect and high intensity. Early detection of cerebrovascular disease and recognising its risk factors are crucial to the prevention of clinically manifested cerebral strokes. This is why studying their harmful impact, including their role in the development of asymptomatic forms of cerebrovascular disease, is so important and relevant.

The literary review is detailed and informative. It sources 507 works, 10 of which are in Cyrillic and 497 Latin script, with 60% of the citations being from sources published within the recent 10 years. Dr. Dimitrova's review demonstrates broad knowledge in terms of risk factors for asymptomatic ischemic cerebrovascular disorders. She has summarised data on the effect of modifiable and non-modifiable risk factors for asymptomatic disorders. She has done an in-depth analysis of the data on the effects of occupational factors such as stress, physical workload, long working hours, working posture and others on asymptomatic stroke morbidity. She has studied scientific reports on the effect of work factors on the modifiable risk factors for cerebrovascular disease.

Through her comprehensive and detailed analysis of the literature, the postgraduate has pertinently formulated the purpose of the dissertation – "To study the role of occupational factors in the development of asymptomatic ischemic cerebrovascular disorders in working age patients".

In order to achieve this purpose, the postgraduate has defined herself six specific problems and formed five working hypotheses. They are reasonably phrased and correspond to the purpose of the study.

The object of study were 151 patients divided into two groups. The first group consists of 41 patients with vascular risk factors and no history or clinical data of stroke or TIA, with changes on MRI characteristic of asymptomatic cerebrovascular disease. The other group consists of 110 patients with vascular risk factors and no history or clinical data of stroke or TIA, without changes on MRI. The participants were examined, their vascular and behavioural risk factors were established (through medical documentation and survey), their detailed medical history was taken (through survey). Laboratory and neuroimaging (MRI) tests were run for the purposes of the study. The following assessment scales were used: The Workplace Stress Scale (WSS); Montreal Cognitive Assessment Test (MoCA) to assess cognitive impairment; Patient Health Questionnaire-9 (PHQ-9) to assess depression severity.

The statistics methods provide a complete and credible assessment of the data as per the purpose of the study.

The postgraduate has pertinently summarised and illustrated, using tables and figures, the distribution of patients in both groups, and the study results. Processing the demographic and general data of the patients has showed no statistically significant difference between the two groups. The only significant difference being the average age of the participants – it being higher in the group with changes on MRI.

The results prove that hypertension disease, diabetes and ischemic heart disease correlate to changes in MRI and are indicative of increased risk. A correlation was found between changes in MRI and longer professional experience, a longer work week, position, working outside. A higher risk of lesions found in MRI has been calculated for persons with work experience between 20-30 years and 31-40 years, as compared to patients with 10-20 years of work experience. The group with lesions found in MRI have a statistically significant higher average of working hours per week, where working >55 hours per week increases the risk of asymptomatic lesions. Most occupational factors (work experience, working hours/week, working posture, burden of labour) are linked with the presence of hypertension disease. The presence of organic solvents, gasses, noise and vibrations in the work environment statistically correlates to data on changes on MRI. Patients with changes on MRI score significantly higher on stress-scale assessments and the higher values are indicative of a higher risk of lesions on MRI. No statistically significant link has been found between MoCA results of the two groups, i.e. changes in cognition.

The discussion of the results highlights their significance by comparing them with other studies in literature. The conclusion summarises the main results of the study. Eight clearly phrased conclusions were formulated, providing a succinct summary of the results of the study and fulfilling the set purpose and goals. The postgraduate has noted the contributions of the dissertation – four original ones and four affirming.

Dr. Dimitrova has published three full-text publications in Bulgarian periodical journals related to the topic of the dissertation, for two of which she is first author, she has also participated in five scientific forums.

The abstract of the dissertation is compliant with the requirements and its contents correspond to the dissertation. There are 10 tables, 16 figures and 5 appendices illustrating the research results.

Conclusion

Dr. Vladina Miroslavova Dimitrova's dissertation is a well-structured, excellently conducted and analysed study on the effects of modifiable and non-modifiable occupational risk factors for asymptomatic forms of cerebrovascular disease confirmed on MRI. It consists of results and conclusions with original contribution to science and is compliant with all requirements of the ADASRB (Act for the Development of the Academic Staff in the Republic of

Bulgaria), RAADASRB (Regulations for the Application of the Act for the Development of the Academic Staff in the Republic of Bulgaria) and Regulations at MU-Varna.

The dissertation shows that Dr. Dimitrova has wide theoretical and clinical knowledge, has qualities and skills to conduct independent valuable studies, which is why I vote with conviction to award the educational and scientific degree "Doctor" of Medicine to Vladina Miroslavova Dimitrova-Kirilova MD.

09.03.2023

assoc. prof. Kosta Kostov, MD, PhD