

To the Chairman of the Scientific Jury
according to a decision of the Scientific Council
of Acibadem City Clinic UMHAT Tokuda EAD Sofia from 06.11.2024.
(Protocol No. 54/06.11.2024)
and Order No. 15-05-147/20.11.2024
of the Executive Director and the Procurator of the Hospital

STATEMENT

about the dissertation of Dr. Stanislava Lyubomirova Ilieva

on the topic: "Role of some pathogenetic and genetic factors for the development of diabetic nephropathy in patients with type 2 diabetes mellitus" for awarding the degree of Doctor in the field of higher education 7. Health and Sports, professional field 7.1. Medicine, PhD program "Internal Medicine".

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Diabetes mellitus (DM) is recognized as one of the most significant health problems on a global scale. It is among the top 10 causes of premature death, along with cardiovascular, respiratory and malignant diseases. The problem appears not only because the large number of diabetics with CKD, but also because the diagnosis of renal impairment becomes at an advanced stage, with minimal therapeutic response options - diabetic nephropathy (DM) is a leading reason for starting renal replacement therapy. Early diagnosis of CKD in patients with type 2 diabetes is important for achieving a good therapeutic response and preventing and slowing the progression to end-stage renal disease.

This determines the relevance of the dissertation of Dr. Stanislava Lyubomirova Ilieva, who aims to establish the relationship between specific clinical and laboratory biomarkers and the manifestation of the diabetic nephropathy in patients with type 2 diabetes, with a view to establishing predictors for its development and optimizing the diagnosis of diabetic kidney damage. For the realization of the set goal, 6 main tasks have been formulated clearly and precisely.

The dissertation contains 103 standard pages and is illustrated with 33 tables and 15 figures. The literary reference includes 148 literary sources, of which 15 are in Cyrillic and 133 in Latin.

Dr. Stanislava Lyubomirova Ilieva is well aware of the state of the problem and has presented a

creative assessment of the analyzed literary material.

The dissertation covers 91 patients divided into 3 groups: Group I: 30 patients with type 2 diabetes and histologically proven diabetes, group II: 25 patients with type 2 diabetes, in whom there are other, non-diabetic kidney damages in renal histology, group III (control group): 36 patients with histologically proven nephropathies, without diabetes. In almost all patients, percutaneous puncture renal biopsies were performed in the Department of Nephrology of ASK University Hospital - Tokuda. The various modern methods used (clinical, paraclinical, statistical) correspond to the objectives of the study.

The results obtained were interpreted in depth and were compared with the data from studies published in the literature. The analysis of the studied indicators shows that the importance of a specific biomarker pointing to the presence of DM in patients with type 2 diabetes could not be established. This is due to its multifactorial pathogenesis, the manifestation of which is due to the simultaneous action of multiple and different pathogenetic mechanisms. In this sense, the therapeutic approach to diabetic patients should be complex and comprehensive, with a focus on the largest possible number of pathological disorders.

The contributions of the dissertation are of a certain scientific-theoretical and practical nature: 1) for the first time in Bulgaria a study and analysis of many pathogenetic and genetic factors leading to the manifestation of DM has been carried out, 2) the relationship between DM and the polymorphism of the MTHFR-gene, variant A1289C, has been traced, 3) the relationship between DM and thyroid dysfunction has been investigated, and a high incidence of thyroid disorders and autoimmune thyroid diseases in diabetics has been established, 4) the histological verification of renal involvement allows to differentiate diabetic from non-diabetic renal damage in diabetics, establishing the predominance of tubulo-interstitial and vascular damage, 5) the role of puncture renal biopsy as the only reliable diagnostic criterion for DN, as well as for other non-diabetes mellitus-related kidney damage in diabetics, 6) the role of the male sex as a risk factor for DM is established, 7) a widespread carriage of mutant alleles of the MTHFR-gene (1289C and 677T) was found, mainly in a heterozygous form among the studied subjects, who, unlike previous studies, did not show an association with the expression of DN.

In accordance with the with the topic of the dissertation, Dr. Stanislava Lyubomirova Ilieva has 3 presented reports and 3 publications in scientific journals.

The presented materials meet the requirements of the Law on the Development of the Academic Staff of the Republic of Bulgaria and the Regulations for the Development of the Academic Staff of Acibadem City Clinic University Hospital Tokuda EAD Sofia for awarding the scientific degree of "Doctor".

In conclusion, I believe that the dissertation of Dr. Stanislava Lyubomirova Ilieva is complete,

contemporary, in-depth, well-structured and formed, with clear and precisely formulated and completed tasks, with certain conclusions and contributions to both modern science and practice. All this gives me the reason to recommend to the members of the esteemed scientific jury to award Dr. Stanislava Lyubomirova Ilieva the educational and scientific degree of "Doctor" in the scientific specialty of Nephrology in the professional field 7.1. Medicine in the field of higher education 7. Health and sports.

Associate Professor Dr. Alexander Ivanov Osichenko, MD, PhD

06.01.2024

Sofia

