

STATEMENT

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Head of the Ocular Diseases and Vision Sciences Department,
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Medical University "Prof. Dr. Paraskev Stoyanov" – Varna

Member of the Scientific Jury according to Order № R-109-1/ 05.01.2023 of the Rector of the Medical
University "Prof. Dr. Paraskev Stoyanov" – Varna

FOR DISSERTATION PAPER

ON THE SUBJECT:

"In vivo microstructural analysis of rare eye diseases with modern technologies"

FOR AWARD

ON EDUCATIONAL AND SCIENTIFIC DEGREE "DOCTOR"

TO MARIYA RUMENOVA BOYADZHIEVA, MD

Dr. Boyadzhieva was born in 1983 in Sofia. He finished his secondary education in 2002 in Blagoevgrad with a nature-mathematics focus. In 2009, she graduated from the Medical University "Prof. Dr. Paraskev Stoyanov" - Varna. Since 2009 she worked in emergency medical care and reception emergency department, and a year later became part of the team of the Intensive Respiratory Department of University General Hospital for Active Treatment "St. Marina" - Varna. In 2016 she began specialization in "Eye Diseases" at "Specialized Hospital for Eye Diseases for Active Treatment - Varna" ("SHEDAT-Varna"), from 2017 she works as a part-time assistant at the Department of Eye Diseases and Visual Sciences, and since 2018, after passing a competitive exam, she has been appointed as an assistant and became a PhD student. She acquired a specialty in ophthalmology in the December session of 2020. Dr. Boyadzhieva has attached a reference for participation in scientific meetings and conferences in the country and abroad. There are certificates for the following international courses:

- Orthokeratology Course – Paris (2019);
- Summer school in Linshopin under the guidance of Prof. Nil Lagali (2017). There are 17 scientific publications in national and international journals, of which 3 are related to the dissertation work, and 19 citations. She is part of the team of authors of a textbook on "Ocular Diseases" for medical and dental students.

Actuality of the problem

According to the definition of the European Union (EU) Working Group on Rare Diseases, a disease that affects no more than 1 in 2,000 EU citizens is considered rare. More than 7,000 rare diseases are known to date, of which more than 900 are rare eye diseases. Over 70% of rare diseases are genetic. Rare diseases are a public health burden due to the severity of their manifestations and the total number of people they affect. In modern medicine, the focus is not only on the treatment of individual nosological entities, but also on increasing the quality of life of patients. The work of Dr. Maria Boyadzhieva is extremely relevant and timely, as thanks to her work, aniridia was the second eye disease included in the list of rare diseases in Bulgaria. This is a unique development, for which a lot of effort has been put, because in Bulgaria eye diseases during the development of the dissertation were not present in the list of the Ministry of Health.

Dissertation structure

The structure of the dissertation is in accordance with the requirements. The dissertation covers 157 standard pages and is illustrated with 14 tables and 46 figures. The paper includes the following sections: Contents – 1 page, Introduction – 3 pages, Abbreviations used – 1 page, Summary – 3 pages, Abstract – 3 pages, List of figures and tables – 5 pages, Literature review – 36 pages, Aim, tasks and hypotheses – 1 page, Materials and methods – 31 pages, Results – 38 pages, Discussion – 7 pages, Conclusion – 1 page, Conclusions – 2 pages, Contributions – 1 page, List of publications – 1 page, Bibliography – 8 pages, Appendix – 14 pages.

The literature reference includes 142 literary sources (125 in Latin and 17 in Cyrillic), of which 68 were published after 2017.

The literature review begins with a discussion around the definition of rare diseases, which is not refined and summarizes the prevalence and incidence of rare diseases. The accent is placed on the sources of information and data on rare diseases with a precise analysis of eye diseases with their clinical picture. Attention is paid to the diagnosis, treatment and prevention of rare diseases and rare eye diseases, as well as the place and role of specialists and patient organizations.

The aim of the dissertation work is "tracking the path of patients with rare eye diseases, evaluating the registration regime, including eye diseases in the national registry for rare diseases and creating a clinical registry model for the benefit of daily ophthalmic practice". To achieve the goal, 6 tasks have been formulated as follows:

1. Overview of the European rules and registration regimes for rare diseases and rare eye diseases. Review of the National Rare Disease Registry.
2. Assessment of knowledge about rare diseases among ophthalmologists.
3. Creation of a model for registration of a rare eye disease - Aniridia.
4. Clinical evaluation of rare eye diseases according to the Orphanet classification.
5. Creation of a model for a publicly available national register for rare eye diseases in Bulgaria.
6. Development of a plan to create an expert center for rare eye diseases in Bulgaria.

The work schedule of the dissertation covers a 5-year period from 2017 until 2022 and a thorough review of the published literature and publicly available data on rare diseases was performed. This includes rare eye diseases, as well as tracking patients with rare eye diseases using innovative technology such as live confocal microscopy and optical coherence tomography. Criteria for inclusion and exclusion from the study have been determined, and the methodology includes a documentary method, a survey method, modeling and clinical research - clinical methods for evaluating rare eye diseases. The first questionnaire in Bulgaria was created to study the knowledge and exposure of ophthalmologists to rare diseases.

The results prove that in the field of rare diseases, well-maintained and properly systematized registries are extremely valuable. The author emphasizes that local epidemiological data on rare diseases in our country are practically absent. The registries established for a very small number of rare conditions at the hospital level and/or at the centers of expertise and patient associations for rare diseases are insufficient to generate the necessary health information. The most disturbing fact is that Bulgaria does not have an expert center for rare eye diseases and a register of patients with rare eye diseases, which is why the author is developing an algorithm for registration of an expert center and a clinical register for rare eye diseases. The inclusion in the national list of rare diseases of a rare eye disease - Aniridia is a fundamental step in this direction. The analysis of the questionnaires (out of 110 sent, correctly completed and 74 returned) regarding the awareness of Bulgarian specialists and post-graduate students

in "Eye Diseases", shows that nearly half of the respondents meet a patient with a rare eye disease every month, but only 39.47% of those who completed the questionnaire treat these patients. It is interesting to note that nearly 60% of the respondents are of the opinion that Bulgarian doctors and ophthalmologists do not receive professional training for the prevention, diagnosis and treatment of rare diseases, although 60% of the respondents say that during their training they had specific classes/lectures dedicated to these diseases. It is noteworthy that specialists emphasize the need to create a registry and centers for rare diseases.

A prospective tracing of 39 patients was performed according to algorithms created in the present study for the follow-up of rare eye diseases. From the analysis of the accumulated data, it is clearly seen that the algorithms created by the author will help to collect qualitative and analytical data, implement control over the disease, and report the effect of the conducted treatment - a basis for creating standards for good medical practice.

The discussion is again focused on the importance of rare eye diseases as a global problem, the lack of specific health policies and the lack of expertise in the field at the global level, leading to additional physical and psychological suffering for patients and their families.

The scientific work ends with a summary and 10 conclusions, fully answering the set tasks, of which the most important of them are:

1. Based on the conducted extensive and analytical analysis of the data, the need to include more rare eye diseases in the National List of Rare Diseases has been proven.
2. The analysis of the European rules and registration regimes for rare diseases and rare eye diseases proved the need to build a new national program for rare diseases, supporting the National Register of patients with rare diseases and updating Decree No. 16 of 2014 of the Ministry of Health, in line with European legislation.
3. The study confirms the need for the participation of Bulgaria and a Bulgarian expert center for eye diseases in the European reference networks for improving the care and diagnosis of rare eye diseases.
4. It is necessary to update the standard on "Medical genetics", Decree No. 26 of the Ministry of Health and the diagnostic algorithms and indications for conducting genetic and genomic research.

The problem with rare diseases, in particular with rare eye diseases, is not only at the national, but also at the global level, and the lack of a uniform standard and algorithm for diagnosis, tracing and treatment greatly complicates both patients and medical specialists. The work of Dr. Maria Boyadzhieva "In vivo microstructural analysis of rare eye diseases with modern technologies" is modern and up-to-date, meets all the requirements for a dissertation work and marks the beginning of a difficult path that some specialties in Bulgaria have already taken. I have known the PhD student since her first steps in ophthalmology and I think that the development of her academic career with an accent on rare diseases deserves admiration.

I vote positively and recommend to the respected scientific jury in Ophthalmology at the Medical University "Prof. Dr. Paraskev Stoyanov" – Varna to support the awarding of an educational and scientific degree "Doctor" to Dr. Maria Boyadzhieva.

05.06.2023

Varna

Chairman of the Scientific Jury:

Cor. Member Prof. Hristina Grupcheva, MD, PhD, DSc
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