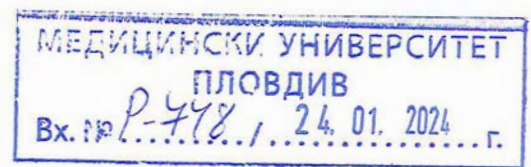


REVIEW



by Prof. Dr. Stoyanka Georgieva Vladeva, dm
Faculty of Medicine, Thrace University, Stara Zagora,

of a dissertation for awarding the educational and scientific degree 'doctor'

professional direction 7.1. Medicine

doctoral program Endocrinology

Author: Dr. Dimitar Manolov Troev

Form of doctoral studies: open doctoral studies

Department: "Endocrinology, Faculty of Medicine, Medical University - Plovdiv

Topic: "CHRONIC AUTOIMMUNE THYROIDITIS OF HASHIMO AND
CO-MORBIDITIES"

Scientific supervisors:

Prof. Dr. Maria Orbetsova, MD, Endocrinology Department, Faculty of Medicine, Medical
University - Plovdiv

Prof. Dr. M. Geneva-Popova, MD , Department of Propaedeutics of Internal Diseases "Prof Dr
Anton Mitov", Faculty of Medicine, Medical University - Plovdiv

1. General presentation of the procedure

The presented set of materials on paper and electronic media is in accordance with Art. 70 (1) of I. Section, Acquisition of the educational and scientific degree "doctor" at MU-Plovdiv; Regulations of MU-Plovdiv dated 28.01.2021 and includes the entire package of required documents. The PhD student has attached 9 full-text publications and 7 scientific communications.

2. Brief biographical data for the doctoral student

Dr. Dimitar Manolov Troev was born on 06.12.1964. He graduated from secondary education at ESPU "Dimitar Blagoev" - Plovdiv in 1982. The doctoral student graduated as a doctor in 1990 at the Medical University of Plovdiv. Since 1991, he has occupied the position of doctor-assistant at the same university, Department and Clinic of Endocrinology and metabolic diseases. He is currently the Department's Chief Administrative Assistant. Dr. Troev has acquired clinical specialties - internal medicine, endocrinology and many additional highly specialized qualifications.

3. Relevance of the dissertation topic

Hashimoto's thyroiditis is the most common autoimmune thyroid disease of any age, and its incidence has been increasing in recent decades. Hashimoto's thyroiditis has been shown to be associated with other autoimmune diseases, which have a wide spectrum according to studies, ranging from involvement of endocrine or non-endocrine organs. Hashimoto's thyroiditis is part of the autoimmune polyglandular syndromes involving multiple endocrine glands such as the pituitary gland, adrenal glands, and parathyroid glands. Over the years, the medical literature has looked for the interrelationships between thyroid gland pathology and inflammatory joint diseases, for example, rheumatoid arthritis. And although this question was studied in the past, in recent years there is no current data in the scientific rheumatological literature about it.

Most of the studies reported in the research literature that evaluated different constellations of autoimmune diseases examined the prevalence of Hashimoto's thyroiditis in nonthyroidal autoimmune diseases, not the other way around.

In Bulgaria, no large-scale study has been conducted characterizing co-morbidities in Hashimoto's thyroiditis. In this sense, the dissertation, which is dedicated to studying the type and frequency of autoimmune and non-autoimmune diseases associated with Hashimoto's autoimmune thyroiditis in the Bulgarian population in hospitalized patients, is modern and relevant.

4. Knowing the problem

The PhD student shows very good theoretical preparation by presenting a thorough and well-structured literature review in 42 pages. Current epidemiological data on the autoimmune nature of Hashimoto's thyroiditis are presented in detail. It is also emphasized that genetic predisposition, environmental factors and internal factors can be crucial in determining the variety of autoimmune manifestations. General data and meta-analyses on the topic include both the most common association with rheumatic diseases and the role of the intestinal epithelium, specifically zonulin, in intestinal permeability. Thus, the author focuses on the new aspect of the relationship between autoimmune thyroid diseases and increased intestinal permeability, respectively the intestinal microbiota and the thyroid gland.

The bibliographic reference of 12 pages includes 460 literary sources, of which 8 in Cyrillic and 452 in Latin. This once again emphasizes the necessity of conducting the present scientific study.

5. Characterization and evaluation of the dissertation work

The dissertation contains 180 standard pages, 29 tables and 33 figures.

In the dissertation, the doctoral student defines a solid objective related to the assessment of associated diseases in hospitalized patients with proven Hashimoto's autoimmune thyroiditis. The objective contains four items and corresponds to the number of studies conducted in the study population.

To fulfill the set goal, Dr. Troev defines eight scientific research tasks. The tasks are specific, feasible and meet the demand in the dissertation work. Each of the studies has a detailed description of design, methods and criteria covering 19 pages.

Data processing and analysis were performed with modern methods such as the statistical package SPSS version 19.0 (Chicago, IL, USA), and for graphical analysis – MS Office Excel 2013.

The results and conclusions are presented in 109 pages.

The dissertation provides valuable results regarding the spectrum of co-morbidities in Hashimoto's thyroiditis (n=447), the most common of which are diabetes mellitus type 1 (n=67), rheumatoid arthritis (n=180), systemic lupus erythematosus, pernicious anemia, vitiligo, carbohydrate and lipid disorders, etc. Even in the initial sample, they appear with a greater frequency than those reported in the general population. The search for predisposing and risk factors for the appearance of associated diseases in Hashimoto's thyroiditis is of great practical importance.

Data on zonulin, studied in a sample of 106 patients with Hashimoto's thyroiditis, are the first for Bulgaria. The relationship of this biomarker of increased intestinal permeability, the levels of which are found categorically higher in carriers of autoimmune thyroid disease compared to the norm and to the control group, with the functional and immunological status of the thyroid gland is still the subject of a worldwide study. Data from the present study found that patients with Hashimoto's thyroiditis had significantly higher levels of serum zonulin compared to reference values in a healthy population, suggesting impaired intestinal permeability in this autoimmune disease.

A study on the combination of rheumatoid arthritis and Hashimoto's thyroiditis in a representative sample of 180 individuals also has a great practical contribution regarding the follow-up of thyroid autoantibodies and thyroid function in patients with newly diagnosed rheumatoid arthritis. The role of thyroiditis on joint destruction at the beginning and at different durations of rheumatoid arthritis was also evaluated. There was no significant association of autoimmune thyroiditis with disease activity, either at the onset or in the evolution of rheumatoid arthritis, but more pronounced radiographic joint changes were observed in the first three years.

The discussion is critical, summarizing and comparing the results obtained by the doctoral student with globally presented ones and looking for the reasons for differences. It was done after the results were presented in each of the individual studies. Separate concrete conclusions have been made for each section, emphasizing the target achievements and facts.

The doctoral student has formulated sixteen summary conclusions, which are properly reasoned and correspond to the set goal and completed tasks. They synthesize the review data analysis of the entire own study.

6. Contributions and significance of the dissertation for science and practice

I accept the contributions, defined respectively as 5 contributions of an original nature, 4 - of a confirmatory nature, 4 - of a scientific-theoretical nature and 2 - of a scientific-applied nature, which objectively reflect the significance of the obtained results in a scientific plan and their applicability in real life clinical practice.

7. Evaluation of publications on the dissertation work

In connection with the dissertation, 9 full-text publications and 7 publications from participation in scientific forums were made. The number of scientific papers is fully sufficient for the quantitative criteria laid down in the Regulations of the MU - Plovdiv for the defense of a doctoral scientific degree.

8. Personal participation of the doctoral student

The long-term clinical, academic and teaching work of Dr. Troev in the field of endocrinology and the presented topic is indisputable. In the conducted dissertation research, including in the scientific publications, the obtained results are obviously the merit of the doctoral student. Two scientific projects have been implemented on the subject, in which Dr. Troev took part as a researcher.

9. Author's abstract

The abstract presents the objectives, tasks, results and discussion, conclusions and contributions of the dissertation work in a concise, summarized form. The results are displayed graphically for greater demonstrability. The abstract gives an overall idea of the obtained results, conclusions and contributions of the dissertation work. It consists of 72 pages.

10. Critical remarks and recommendations

I have no critical remarks or recommendations.

CONCLUSION

The dissertation contains scientific, scientific-applied and applied results, which represent an original contribution to science and meet all the requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria (DASRBA), the Regulations for the Implementation of DASRBA and the relevant Regulations of the Medical University - Plovdiv. The presented materials and dissertation results fully correspond to the specific requirements of the MU - Plovdiv.

The dissertation shows that the doctoral student Dr. Dimitar Manolov Troev has in-depth theoretical knowledge and professional skills in the scientific specialty of endocrinology, demonstrating qualities and skills for independent conduct of scientific research.

Due to the above, I confidently give my positive assessment of the conducted research, presented by the above-reviewed dissertation work, author's abstract, achieved results and contributions, and I propose to the honorable scientific jury to award the educational and scientific degree "doctor" to Dr. Dimitar Manolov Troev in a doctoral program in Endocrinology.

24. 01. 2024

Reviewer:

Залчено на основание
Чл.5 §1, 6."В" Регламент (ЕС)2016/679

Prof. Dr. Stoyanka Vladeva, MD