

## REVIEW

To the dissertation for awarding the educational and scientific degree "Doctor"

on

**Martina Todorova Yaneva MD**

on the topic: **"Etiopathogenetic factors in nummular eczema"**

**Supervisor:** Prof. Dr. Razvigor Darlenski, PhD

**Reviewer:** Assoc. Prof. Dr. Karen Loris Manuelyan, MD

### **Biographical data**

Dr. Martina Todorova Yaneva was born on September 25, 1992 in the city of Sofia. Veliko Tarnovo. She completed her higher education at the Medical University - Sofia, where in 2018 she acquired an educational and qualification degree "Master" in medicine.

After graduation, she began a specialization in Skin and Venereal Diseases at the Clinic of Skin and Venereal Diseases at Acibadem City Clinic University Hospital "Tokuda" - Sofia, which she successfully graduated in 2023, acquiring a specialty in dermatology and venereology.

In parallel with her clinical training, in 2024 Dr. Yaneva also acquired an additional master's degree in Public Health and Health Management, which expanded her competencies in the field of the health system and the organization of medical care.

Her professional path is associated with active clinical practice in the field of dermatology.

Dr. Yaneva demonstrated pronounced scientific activity. She is the author and co-author of numerous scientific publications in Bulgarian and international journals covering topics such as atopic dermatitis, contact hypersensitivity, drug-induced skin reactions and nummular eczema.

She actively participates in national and international scientific forums, including congresses of the European Academy of Dermatology and Venereology (EADV), the American Academy of Dermatology (AAD) and the European Academy of Allergology and Clinical Immunology (EAACI), where she presented the results of her scientific activities in the form of oral presentations and posters.

Her professional development is complemented by participation in a number of specialized courses and trainings in the field of dermatoscopy, dermatoallergology and dermatosurgery, organized by leading international organizations.

Dr. Yaneva is fluent in several foreign languages, including English and French at level C1, German at level B2 and Spanish at level B1, which allows her to actively participate in the international scientific community.

She is a member of a number of professional organizations, including the Bulgarian Dermatological Society (BDD), the European Academy of Dermatology and Venereology (EADV), the European Academy of Allergology and Clinical Immunology (EAACI), the World Allergy Organization (WAO) and the International Dermoscopy Society.

All these data outline the profile of a young but already established specialist with active scientific and clinical activity, which creates a good basis for the implementation of the dissertation.

### **Relevance of topic**

The dissertation is dedicated to an extremely relevant and still insufficiently clarified problem in modern dermatology – the etiopathogenesis of nummular eczema.

As emphasized in the introduction of the work, nummular eczema is a chronic, recurrent dermatological disease with a complex and not fully understood pathogenesis. Although it occurs relatively frequently in clinical practice, it remains poorly defined in terms of etiological factors, making it difficult to carry out targeted treatment.

Of particular importance is the fact that the disease leads to a significant deterioration in the quality of life of patients, both due to chronic itching and skin manifestations, as well as due to social and psychological consequences.

Against this background, the study of the multifactorial genesis of the disease, including the role of atopy, contact sensitization, microbiological factors and disorders in the skin barrier, is essential both from a scientific point of view and for clinical practice.

### **Structure and volume of the dissertation**

The dissertation has a volume of 160 pages with 60 figures and 35 tables and is structured according to the approved academic requirements.

The main sections are included – introduction, literature review, formulation of purpose and objectives, materials and methods, results, discussion, conclusions, contributions, as well as bibliography and appendices. The bibliography contains a total of 184 sources.

The Literature Review covers a wide range of scholarly publications, with the bibliography including 184 sources, 24 with Bulgarian authors and 160 with foreign authors.

The structure of the work is logical, consistent and makes it easy to follow up on the scientific idea and the results achieved.

### **Scientific validity and knowledge of the topic**

The PhD student demonstrates in-depth knowledge of the topic. The literature review discusses the main etiopathogenetic factors, such as atopy and its relationship with nummular eczema, drug-induced dermatoses, contact hypersensitivity, cutaneous xerosis, bacterial colonisation, vascular and trophic disorders, as well as neuroimmunological mechanisms.

Especially valuable is the attempt to systematize these factors in a single pathogenetic model. The PhD student is not limited to a descriptive approach, but makes a critical analysis of the different hypotheses, looking for the relationships between them.

For example, the role of contact allergy and its frequency in patients with nummular eczema, as well as the possibility of drug-induced forms of the disease, are clearly considered.

### **Materials, methodology and results**

The dissertation is based on an observational, cross-sectional clinical study conducted at the Clinic of Skin and Venereal Diseases at Acibadem City Clinic University

Hospital "Tokuda", Sofia. Sofia. The study included 184 patients – 84 with clinically diagnosed nummular eczema and 100 patients with other types of dermatitis, in whom standardized clinical, allergological and paraclinical assessment was performed.

Data have been collected on the main demographic indicators, the clinical characteristics of the disease, as well as on the presence of predisposing factors such as atopy, xerosis, drug exposure and concomitant diseases. A detailed assessment of the skin status was carried out, analyzing the localization, morphology and distribution of the lesions.

To objectify the severity of the disease, an assessment scale has been introduced and applied, allowing quantitative analysis and comparability of the results. In parallel, patient-oriented indicators (PROs) were assessed, with itching, sleep disturbance, and skin dryness measured by a visual-numerical scale (VCS) and quality of life by a validated 10-question questionnaire.

The allergy assessment included patch testing with standard allergen series, and the results were compared with control groups of patients with other forms of dermatitis. The role of bacterial antigens has been further analyzed by conducting intradermal in vivo skin tests, which represents an innovative approach in the context of the disease.

The statistical processing of the data is carried out by applying methods of descriptive and analytical statistics. A  $\chi^2$ -test was used to assess the dependence between categorical variables, correlation analyses (Spearman) to establish relationships between quantitative indicators, as well as methods for estimating statistical significance at level  $p < 0.05$ . The data are processed with specialized statistical software, which guarantees the reliability of the results obtained.

The results show that nummular eczema is a disease of multifactorial genesis and heterogeneous clinical manifestation. Statistically significant relationships have been established between the severity of the disease and the presence of certain etiopathogenetic factors, including xerosis and bacterial colonization.

The analysis of contact sensitization shows a significant proportion of positive patch tests, and the results obtained correspond to published data on the incidence of contact allergy in patients with nummular eczema. There is a statistically significant relationship between the presence of sensitization and the chronic course of the disease.

The results of intradermal tests support the role of bacterial antigens as a potential trigger in pathogenesis, taking into account a link between positive tests and more severe clinical presentation.

The analysis of patient-centered indicators showed a moderate to strong correlation between itching intensity, sleep disturbance, and overall quality of life, highlighting the significant impact of the disease on patients' daily functioning.

In summary, the methodology used is reliable, valid and consistent with the goals and objectives. The results obtained are statistically substantiated and contribute to a better understanding of the etiopathogenetic mechanisms in nummular eczema, having the potential for direct application in clinical practice.

### **Scientific and practical contributions**

The dissertation contains original scientific and practical contributions with a pronounced clinical orientation.

The main contribution should be pointed out as the complex analysis of etiopathogenetic factors in nummular eczema, and for the first time within the Bulgarian population, the role of contact hypersensitivity, bacterial antigens and disorders in the skin barrier is simultaneously studied. This allows for a more precise definition of the multifactorial nature of the disease.

A significant contribution is the introduction and application of the NESI (Nummular Eczema Severity Index) scale to assess the severity of the disease, which provides an objectified and reproducible method for quantification and follow-up in clinical practice.

A systematic study of patient-oriented indicators (PROs), including assessment of pruritus, sleep disturbance, and quality of life through a visual-numerical scale and a validated questionnaire, has also made a contribution, and a correlation between subjective symptoms and clinical severity has been established.

A significant frequency of contact sensitization through epicutaneous testing has been proven, which justifies the need for routine patch tests in patients with nummular eczema and has a direct impact on the diagnostic approach.

As an original element, the use of intradermal in vivo tests to assess the role of bacterial antigens should also be noted, which complements the existing data on the involvement of microbiological factors in the pathogenesis of the disease.

In practical terms, the results create the basis for an individualized diagnostic and therapeutic approach, including an assessment of allergological status, control of microbiological factors and restoration of the skin barrier.

In summary, the contributions are clearly defined, with scientific novelty and direct application in clinical practice.

## **Publications and academic activity**

The PhD student presented five publications on the topic of the dissertation, being the first author in all of them, including an article with an impact factor. She has participated actively in scientific forums.

## **Conclusion**

The dissertation of Dr. Martina Todorova Yaneva on the topic "Etiopathogenetic factors in nummular eczema", supervisor Prof. Razvigor Darlenski, is correctly and thoroughly executed with well-set goals and tasks. The dissertation uses up-to-date diagnostic methods, and the results are interpreted with reliability.

In the final version of the dissertation, the critical remarks made in my review are taken into account.

I believe that the work meets the requirements of the Academic Staff Development Act, shows theoretical training and scientific and practical potential, and the contributions are original. I recommend the esteemed members of the scientific jury to give their positive assessment, and I propose that Dr. Martina Todorova Yaneva be awarded the educational and scientific degree of Doctor.

Burgas, 05 May 2026

**Reviewer:**



Assoc. Prof. Karen Loris Manuelyan, MD