

REVIEW

By

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Medical Institute, Ministry of Interior – Sofia
External Member of the Academic Jury

Regarding the dissertation thesis entitled:

“Analysis of the Expression of Hormonal Receptors and the Biomarkers p53 and Ki-67 in Endometrial Polyps in Pre- and Postmenopausal Women”

Submitted for the award of the Educational and Scientific Degree "Doctor"

Doctoral Program: *Obstetrics and Gynecology*,

Professional Field: 7.1. Medicine

Area of Higher Education: 7. Health and Sports

Author: Dr. Krum Stefanov Vladov

Full-time PhD student, Department of Obstetrics and Gynecology,

Faculty of Medicine, Medical University – Plovdiv

Scientific Supervisors:

Prof. Ekaterina Uchikova, MD. PhD

Prof. Veselin Belovezhkov, MD.PhD

This review has been prepared in accordance with Order No. R-3342 dated 01.07.2025 for the approval of the Academic Jury for the award of the ESD "Doctor" to Dr. Krum Vladov. It fully complies with the requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria, its Implementing Regulations, and the Regulations for the Development of the Academic Staff at the Medical University – Plovdiv.

Dr. Vladov has submitted all the necessary materials required under the procedure for the defense.

Biographical Data of the Candidate

I would like to highlight a few key facts from the biography of Dr. Krum Vladov. He was born in 1992 in the town of Pazardzhik. He graduated with distinction from the Medical University – Plovdiv in 2017, obtaining the Master's degree in Medicine with the professional qualification "Physician." In November of the same year, he commenced his residency in

Obstetrics and Gynecology at the Department and Clinic of Obstetrics and Gynecology, University Hospital "St. George", Plovdiv.

He also holds an academic position as Assistant Professor, teaching medical and dental students in English. Within the department, he is responsible for research activities, a member of examination committees, and a mentor for student interest groups and summer clinical practice. Since December 2022, he has been enrolled as a full-time doctoral student in the doctoral program in Obstetrics and Gynecology.

Dr. Vladov is a member of the Bulgarian Medical Association and serves on the Committee for Professional Ethics at the Regional College in Plovdiv. He is also affiliated with the Bulgarian Society of Obstetrics and Gynecology, the Bulgarian Association of Oncogynecology, the Bulgarian Association of Minimally Invasive and Robotic Surgery, and the Youth Scientific Society "Asklepios." He is the author and co-author of refereed and indexed publications in both Bulgarian and international journals, and has delivered lectures at various national and international scientific forums.

In connection with the preparation of his dissertation, Dr. Vladov has presented six publications, being the first author in five, one of which has been published in a reputable international journal with an impact factor. He has participated in three national and international scientific conferences and has completed numerous specialized courses related to advancing his professional qualification.

Structure and Characteristics of the Dissertation

The topic concerning the etiopathogenesis of endometrial polyps is highly relevant and of clinical importance. This form of endometrial pathology represents one of the most frequently diagnosed benign lesions of the uterine lining, with increasing prevalence due to the widespread use of transvaginal ultrasonography in current medical practice.

Existing data indicate that hormonal imbalance, particularly elevated serum estradiol levels in pre- and postmenopausal women, as well as the mechanisms of cellular proliferation and apoptosis, play a leading role in the development of endometrial polyps. Modern molecular markers such as the tumor suppressor gene p53 and the proliferation marker Ki-67 are used for assessing the risk of malignant transformation. Investigating their expression alongside the assessment of steroid hormone receptors and serum estradiol levels can significantly aid clinical evaluation and optimize the therapeutic approach in patients with established risk profiles.

The topic, as presented, is timely, of high academic interest, and suitable for a dissertation.

The dissertation manuscript comprises 210 pages and fully meets the formal and structural requirements. The literature review encompasses 196 sources, including 15 in Bulgarian. All references are cited correctly and are up to date, with one-third published within the last five years.

The primary aim of the clinical study is to analyze the expression of estrogen and progesterone steroid hormone receptors, as well as the proliferation and apoptosis biomarkers, in endometrial polyps in pre- and postmenopausal women. Five well-formulated and specific objectives have been defined to achieve this aim.

Under the supervision of leading specialists Prof. Uchikova and Prof. Belovezhkov, the doctoral candidate has conducted a cross-sectional study between 2022 and 2024. It was carried out at the Department of Obstetrics and Gynecology at MU–Plovdiv, the Clinic of Obstetrics and Gynecology at UH “St. George” – Plovdiv, the Department of General and Clinical Pathology at MU–Plovdiv, the Clinic of Pathology at UH “St. George”, the Morphological Research Center at MU–Plovdiv, and the Central Clinical Laboratory at UH “St. George”, underscoring the multidisciplinary character of the work.

A total of 120 women were included, distributed into three groups of 40 each: those with histologically confirmed endometrial polyps, endometrial carcinoma, and atrophic endometrium. The inclusion and exclusion criteria were clearly and precisely defined.

The methods employed in this research are modern, varied, and appropriately applied. The doctoral student utilized classical clinical diagnostic techniques in conjunction with imaging, invasive procedures ranging from minimally invasive diagnostic curettage to more extensive surgeries like abdominal and vaginal hysterectomy. These methods enabled the collection of specimens for histopathological confirmation. The expression of hormone receptors and biomarkers was analyzed through modern immunohistochemical techniques. Contemporary statistical methods were applied for data analysis, ensuring statistical reliability.

The candidate presents original findings in 112 pages, supported by 82 tables and 56 figures. These illustrate demographic data, estradiol serum concentrations, and immunoexpression of hormonal receptors and biomarkers.

Of particular clinical interest is the proposed practical model for risk stratification in patients with endometrial polyps. This model integrates clinical, hormonal, metabolic, and immunohistochemical parameters, allowing personalized risk assessment and aiding clinical decision-making—from observation in low-risk cases to more aggressive management in suspected malignant transformation.

Three hypotheses were formulated, contributing to the theoretical understanding of the etiology of endometrial polyps: hormone-mediated proliferation, localized genetic instability with low proliferative activity, and the role of obesity. All are well-supported by the findings. Six conclusions were derived logically from the stated objectives, with clear clinical and scientific implications.

Scientific Contributions. The dissertation demonstrates a high level of analytical depth and correlates the findings with existing literature. The discussion is structured and addresses various dimensions: age, menstrual and reproductive factors, metabolic syndrome, hormonal influences, abnormal uterine bleeding, smoking, serum estradiol levels, expression of hormone receptors, and biomarkers p53 and Ki-67.

The scientific contributions are original and significant. Particularly noteworthy are: the hypotheses concerning the etiology and pathogenesis of endometrial polyps in pre- and postmenopausal women, the demonstrated biological inertness of the stromal component, and the proposed practical model for risk stratification based on integrated parameters.

Recommendations

1. The doctoral candidate should disseminate the results of this study through publications in internationally indexed and peer-reviewed journals.
2. A monograph based on this dissertation is recommended, which would further promote the originality and practical relevance of the findings.

Conclusion

Dr. Krum Vladov is a promising young researcher and clinician with original scientific ideas and a solid theoretical and practical foundation. He addresses a relevant clinical issue in gynecology. Clarifying the etiology and pathogenesis of endometrial polyps in pre- and postmenopausal women offers the potential for individualized risk assessment and prevention of malignant transformation.

Following a comprehensive review of the dissertation titled: *"Analysis of the Expression of Hormonal Receptors and the Biomarkers p53 and Ki-67 in Endometrial Polyps in Pre- and Postmenopausal Women"*, I express my unequivocally positive opinion of this work. The topic is current and of clinical significance, addressing a common gynecological pathology with potential for neoplastic transformation. The study enriches our understanding of the molecular and histological characteristics of endometrial polyps across different age groups, offering clear diagnostic and prognostic value.

The methodology is precisely selected, professionally applied, and supports reproducibility. The scope of the material studied allows for conclusions with high scientific reliability.

The dissertation makes undeniable scientific contributions. The candidate presents original data on the expression of hormone receptors and proliferative biomarkers, identifying statistically significant differences between age groups. These findings contribute to a deeper understanding of the biological behavior of endometrial polyps and have clear clinical applications.

In light of the above, I conclude that the dissertation fully meets the requirements of the Law on the Development of Academic Staff and the applicable regulations. I give a positive review and firmly recommend the awarding of the Educational and Scientific Degree "Doctor" in the doctoral program *Obstetrics and Gynecology*, Professional Field 7.1. Medicine.

I affirm that this scientific work satisfies the criteria for the award of the ESD "Doctor" and hereby assign a POSITIVE EVALUATION. I recommend the members of the academic jury proceed with the procedure and vote in favor.

Date: 28/07/25

Reviewer:
/Prof. Petar Petrov, MD.PhD/

Заличено на основание
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