

REVIEW

by

Prof. Dr. Elena Dimitrova Dimitrakova, MD

Department of Obstetrics and Gynecology, Medical University of Plovdiv

Head of the Delivery Department, University Multiprofile Hospital for Active Treatment

"St. Georgi" - Plovdiv

Subject: Dissertation titled "Correlation between Ultrasound Diagnosis and Immunohistochemistry in Early and Late Spontaneous Abortions" by Dr. Tsvetomir Evgeniev Kachovski for the award of the academic degree "Doctor," field of higher education: 7. Healthcare and Sports, Professional Field 7.1 Medicine, Doctoral Program "Obstetrics and Gynecology," in accordance with Order No. R-109-350/18.07.2023 issued by the Rector of MU-Varna.

I. BRIEF BIOGRAPHICAL DATA AND CAREER PROFILE OF THE CANDIDATE

Dr. Tsvetomir Kachovski was born in 1989. He graduated as a medical doctor from the Medical University of Pleven. In 2015, he was enrolled as a specialist at University Multiprofile Hospital for Active Treatment "Prof. D. Stamatov" in Varna. In 2019, he obtained a specialty in "Obstetrics and Gynecology." Since 2016, he has been an honorary assistant at the Department of Obstetrics and Gynecology at MU-Varna, and since 2020, a regular assistant. Since 2020, he has been working as a physician in the "Gynecology" department at University Multiprofile Hospital for Active Treatment "Prof. D. Stamatov."

Dr. Kachovski has completed additional training courses both in Bulgaria and abroad, including prenatal ultrasound diagnostics, hysteroscopy, and others. He is a member of several organizations, including BLS, BAUAG, BAMIGH, ISOUG, FMF.

II. SIGNIFICANCE OF THE PROBLEM

The frequency of spontaneous abortions in the first trimester of pregnancy varies between 15-20%. Until recently, genetic deviations, anatomical characteristics, environmental factors, etc., were discussed as leading causes of their occurrence.

In recent decades, the development of specific medical fields has contributed to enriching the knowledge about the etiology of spontaneous abortions. However, this remains frequently unclear.

Contemporary research points to the role of decidual NK cells (dNK) as potential "participants" in this obstetric pathology. Their role in angiogenesis and remodeling of spiral arteries is known. It is also known that disturbances in these processes underlie conditions such as preeclampsia, premature birth, etc. Disturbed angiogenesis, in turn, affects the uteroplacental blood flow, which can be assessed by Doppler velocimetry. Combining this

method with immunohistochemical analysis for the study of spontaneous abortions within the Bulgarian population would enrich existing knowledge. Therefore, I assess the topic of the dissertation as modern and relevant.

The aim of the dissertation is clearly formulated, and the candidate sets 7 well-defined tasks for its fulfillment:

1. Perform and analyze Doppler velocimetry of uterine arteries in early spontaneous abortions and elective abortions up to 12 weeks gestation.
2. Assess the role of immunohistochemistry of dNK cells and proliferative marker Ki67 in early abortions up to 12 weeks gestation.
3. Investigate and analyze the correlation between Doppler velocimetry of uterine arteries and immunohistochemistry of dNK cells and proliferative marker Ki67 in abortions up to 12 weeks gestation.
4. Evaluate Doppler velocimetry of uterine arteries in late spontaneous abortions up to 20 weeks gestation.
5. Determine the role of immunohistochemistry of dNK cells and proliferative marker Ki67 in abortions up to 20 weeks gestation.
6. Perform and analyze Doppler velocimetry of uterine arteries and immunohistochemistry of dNK cells and proliferative marker Ki67 in abortions up to 20 weeks gestation.
7. Realize assessment and analysis of Doppler velocimetry of uterine arteries and immunohistochemical analysis of dNK cells and proliferative marker Ki67 in abortions up to 12 weeks and 20 weeks gestation.

III. STRUCTURE OF THE DISSERTATION

The dissertation follows a classical structure with a well-maintained balance between its individual sections. It spans 160 standard pages and includes a bibliography containing 305 literary sources, with 32 in Cyrillic and 273 in Latin script. The presentation is enhanced by 36 figures and 62 tables.

MATERIALS AND METHODS: The study encompasses 81 pregnant patients and was conducted from October 2018 to January 2023, comprising both retrospective and prospective components. Clinical data from the "Gynecology" department at University Multiprofile Hospital for Active Treatment "Prof. D. Stamatov" in Varna were utilized.

OWN RESULTS: The acquired results were analyzed using a diverse range of statistical methods, yielding information that can be summarized into several key points:

- The majority of spontaneous abortions occur in the first trimester, accounting for 70.9%.
- No statistically significant correlation exists between the age of pregnant women experiencing spontaneous abortion and the expression of Ki67.
- Among patients under the age of 35, a higher percentage exhibits elevated expression of CD56+.

- An increase in gestational age by one week correlates with a rise in Ri values of the uterine and umbilical artery by 0.13/0.12 units and a decrease in Pi by 0.19/0.18 units.
- Early spontaneous abortions display a high percentage of CD56+ and weak expression of Ki67.
- A comparison between early and late abortions reveals a higher percentage of CD56+ in those up to 12 weeks gestation.

The conclusions drawn from the dissertation total 11 and are in strong alignment with the initially defined tasks.

CONTRIBUTIONS OF THE DISSERTATION:

The dissertation presents both original contributions and those with a confirmatory character:

1. For the first time in Bulgaria, a study has been conducted on abortion material using immunohistochemistry with the proliferative marker Ki67 and CD56+ in the first and second trimesters of pregnancy.
2. For the first time in Bulgaria, an investigation and analysis of spontaneous abortions has been conducted through the combined use of two methods: immunohistochemistry and Doppler velocimetry.
3. An exemplary screening algorithm for pregnant women with threatened abortion has been developed.

IV. CONCLUSION

The presented dissertation work is an original and in-depth study. The candidate has demonstrated a sufficient number of publications. It meets the requirements of the Regulations for the Award of Academic Degrees and Titles in the Republic of Bulgaria, the Rules for its Application, and the corresponding Regulations of MU-Varna.

Considering the above, I recommend to the esteemed members of the Academic Jury to vote positively for the award of the academic degree "Doctor" to Dr. Tsvetomir Kachovski.

August 19, 2023 Prepared the review:

Plovdiv, Bulgaria Prof. Dr. Elena Dimitrakova, MD



R E V I E W

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