THREAT OF MISCARRIAGE AT 10–13 WEEKS OF GESTATION: CONSEQUENCES AND POSSIBLE RISKS

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https://doi.org/10.35339/ic.2025.12.4.kov

ABSTRACT

Background. Problems during the fetal period attract our particular attention, as they prevent the second wave of cytotrophoblast invasion into the myometrial segments of the spiral arteries and contribute to the development of placental dysfunction.

Aim. To study the state of extraembryonic structures in case of miscarriage, at the fetal stage of intrauterine development of the child, at the end of the first trimester of gestation and their influence on the development of placental dysfunction.

Materials and Methods. The study included 20 patients (Group 1) with a verified threat of pregnancy termination without bleeding at the fetal stage of gestation ([10–13] weeks), 22 women with verified Retro-Chorial Hematoma (RCH) at the same time (Group 2) and 20 women (Control Group) with a physiological course of the first trimester of gestation. During the transvaginal ultrasound examination, the chorionic volume was calculated using a special three-dimensional program VOCAL (Virtual Organ Computer-aided AnaLysis), and its vascular system was assessed. The data are presented as Me [Q_1; Q_3]; the comparison of three groups was performed by the Kruskal–Wallis test with Dunn's post-hoc test and Bonferroni correction.

Research Ethics. The study was conducted in accordance with the principles of the World Medical Association Declaration of Helsinki (1964–2024) and approved by the Biomedical Ethics Committee of Bukovinian State Medical University (Protocol No.7 of April 17, 2025). The examination was performed only after obtaining the patient's informed consent.

Results. In the Control Group, the median chorionic volume (Vx) was 164.0 [162.5; 165.2] cm^3, the Vascularization Index (VI) was 19.4 [18.3; 20.7], and the blood Flow Index (FI) was 49.2 [48.5; 50.1]. In Group 1 (threat of miscarriage without bleeding), Vx decreased to 152.1 [146.2; 156.8] cm^3 (by 7.4%), VI to 13.4 [12.5; 14.3] (by 30.9%), and FI to 41.3 [39.0; 43.7] (by 16.1%). In Group 2 (threat of retrochorial hematoma), Vx decreased to 131.5 [127.1; 135.9] cm^3 (by 20.1%), VI to 9.6 [8.9; 10.4] (by 50.5%), and FI to 34.1 [31.8; 36.3] (by 30.7%). All differences were statistically significant (Kruskal–Wallis test with Dunn's post-hoc and Bonferroni correction, adjusted $p<0.01$ for Group 1 vs. Control Group, and $p<0.001$ for Group 2 vs. Control Group as well as $p<0.01$ for Group 1 vs. Group 2).

Conclusions. Retrochorionic hematomas formed at the risk of miscarriage at [10–13] weeks of gestation are a direct cause of chorionic hypoplasia and impaired chorionic maturation. A decrease in the index of vascularization and blood flow in the chorion creates a high risk of placental dysfunction, which in turn worsens the prognosis of further pregnancy.

Keywords: *obstetrics, placenta, angiogenesis, ultrasonography, obstetric hemorrhage, trophoblast.*

Introduction

The threat of pregnancy termination, which occurs in the early stages of gestation, significantly affects the formation of the uterine-placental system and the development of placental dysfunction. Both the threat of miscarriage without bleeding and RetroChorial Hematoma (RCH) occur against the background of increased uterine tone. In turn, increased myometrial tone leads to disruption of trophoblast invasion and spiral artery remodeling, which is a prerequisite for the development of placental dysfunction. The frequency of pregnancy loss today does not show a downward trend [1–3]. Moreover, [10–12]% of miscarriages occurs during the embryonic period, and [2–3] % of pregnancies is terminated during the fetal (after 10 weeks) stage of intrauterine development [4–6].

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Problems of the fetal period attract our special attention, since they prevent the passage of the second wave of cytotrophoblast invasion into the myometrial segments of the spiral arteries [7–9]. This results in a lack of adequate growth of uteroplacental blood flow, which in turn leads to an imbalance in the lipid peroxidation system, increased permeability of the placental barrier, and damage to the cell membranes of the developing placenta [10; 11].

Therefore, it is clear that it is necessary to study the effect of the threat of miscarriage in the early fetal period ([10–13] weeks) on the development of placental dysfunction.

Aim of the research was to study the condition of extraembryonic structures (namely, the chorion) in cases of miscarriage, at the fetal stage of intrauterine development of the child, at the end of the first trimester of gestation, and their impact on the development of placental dysfunction.

Materials and Methods

Twenty patients (Group 1) with a verified threat of pregnancy termination without bleeding at the fetal stage of gestation ([10–13] weeks) were observed, 22 women with verified RCH at the same stage (Group 2), and 20 women (Control Group) with a physiological course of the first trimester of gestation. The exclusion criteria were patients with induced pregnancy, multiple pregnancies, and abnormalities in the development of female reproductive organs, as well as patients with extragenital pathology (arterial hypertension, diabetes mellitus, kidney diseases, autoimmune diseases) that could affect the condition of the chorion.

The study groups were representative in terms of age, social status, and somatic history.

All pregnant women underwent a comprehensive clinical and laboratory examination. During a transvaginal ultrasound examination at the end of the first trimester of pregnancy ([12–13] weeks), the volume of the chorion was calculated and its vascular system was assessed using a special three-dimensional VOCAL (Virtual Organ Computer-aided AnaLysis) program (GE Healthcare / Kretztechnik AG, Austria). Volumetric blood flow indicators of the chorion were evaluated using automatic calculation of Vascularization Index (VI) and blood Flow Index (FI).

Statistical analysis was performed using the Statistica 13.0 (TIBCO, USA). The distribution of quantitative variables was checked for normality using the Shapiro–Wilk test. Since the distribution of indicators in the groups differed from normal, and the sample size was small ($n \leq 22$), non-parametric methods were used for further analysis. Data are presented as median and interquartile range: Me [Q1; Q3].

The Kruskal–Wallis H-test was used to compare three independent groups. When statistically significant differences ($p<0.05$) were detected, post-hoc comparisons were performed using Dunn's test with Bonferroni's correction for multiple tests. Differences were considered statistically significant at adjusted $p<0.05$.

Research Ethics

The study was conducted in accordance with the principles of the World Medical Association Declaration of Helsinki (1964–2024) and approved by the Biomedical Ethics Committee of Bukovinian State Medical University in accordance with the moral and legal rules for conducting medical research (Protocol No.7 of April 17, 2025). The examination was performed only after obtaining the patient's informed consent.

Results

The age of women in the studied groups practically did not differ: Group 1 – 25.8 [23.0; 28.0] years, Group 2 – 26.7 [24.1; 29.5], Control Group – 27.2 [23.0; 31.0] ($p>0.05$ according to the Kruskal–Wallis test).

Seventeen patients (85.0%) in Group 1 had repeated pregnancy, in Group 2 this figure was 81.8% (18), and in the Control Group 75.0% (15). Approximately the same frequency of Complicated Obstetric History (COH) was found in Group 1 and Group 2, 9 (45.0%) and 10 (45.4%), respectively. In pregnant women with uncomplicated first trimester gestation, COH was observed in 3 cases (15%). A detailed analysis of the obstetric and gynecological history revealed that the frequency of spontaneous abortions in Group 1 was 3 (15.0%) and in Group 2 – 5 (22.7%), while it was significantly lower in the Control Group, 1 (5.0%) of cases. A history of inflammatory diseases was noted in 2 patients (10.0%) of Group 1 and 4 patients (18.2%) of Group 2. In the Control Group, this indicator was 1 (5.0%). One (4.5%) pregnant women in Group 2 had surgical interventions on the abdominal organs. In Groups 1 and the Control Group, the subjects denied having undergone surgical interventions.

Cervical erosion was found in the examined groups with almost the same frequency: 2 (10.0%), 3 (13.6%), and 2 (10.0%), respectively. Menstrual cycle disorders were noted in 3 (15.0%) patients of Group 1, 5 (22.7%) patients of Group 2, and 1 (5.0%) patient in the Control Group. In

Group 2, 2 (9.0%) pregnant women reported a history of premature birth. In Group 1 and the Control Group, all multiparous women had full-term and physiologically normal deliveries.

All women examined in Group 1 and Group 2 were admitted to the hospital at [10–13] weeks of pregnancy with the signs of threatened miscarriage: all complained of aching pain in the lower abdomen. Pregnant women in Group 2 also noted minor bloody discharge from the genital tract, which lasted from 3 to 6 hours before admission. All patients underwent transvaginal ultrasound examination, during which women in Group 2 were diagnosed with segmental contraction of the myometrium and retrochorial hematoma ranging in volume from 0.080 cm^3 to 2.721 cm^3.

The average hematoma volume was [1.3±0.31] cm^3. In pregnant women in Group 1, ultrasound signs of increased uterine tone were verified in only 17 (85.0%) of cases. All diagnosed RCHs were of corporal localization, which, as a rule, does not correlate with the risk of spontaneous abortion.

At [12–13] weeks of gestation, pregnant women of all three groups were examined for Vx, the medians of which are shown in the *Table 1* and *Table 2*. In patients of the Group 1, the volume of the chorion was smaller compared to the control (adjusted $p<0.01$), in the patients of the Group 2 it was even smaller (adjusted $p<0.001$ compared to the Control Group and $p<0.01$ compared to the Group I).

The VI of the chorion (ratio of the vascular component and parenchyma) in pregnant women of the Group 1 was 13.4 [12.5; 14.3], in the Group 2 – 9.6 [8.9; 10.4], which was significantly lower than the Control Group (19.4 [18.3, 20.7]; adjusted $p<0.001$).

Blood FI was also significantly reduced in the group with CKD: 34.1 [31.8; 36.3] compared to the Control Group (49.2 [48.5, 50.1]; adjusted $p<0.001$) and to the Group I (41.3 [39.0; 43.7]; adjusted $p<0.01$).

A significant decrease in all indicators was observed in pregnant women in Group 2, where the threat of miscarriage at [10–13] weeks was accompanied by the formation of RCH (*Table 2*).

The volume of the chorion was reduced by 20.1%, the VI by almost 50.0%, and the blood flow index by 30.7%.

A pairwise comparison of experimental groups (1 and 2) confirmed statistically significantly lower

Table 1. The state of the chorion at the threat of miscarriage without bleeding at 10–13 weeks of gestation.

Examined groups	n	The volume of the chorion (Vx, cm^3)	Vascularization index (VI)	Blood flow index (FI)
Control Group	20	164.0 [162.5; 165.2]	19.4 [18.3; 20.7]	49.2 [48.5; 50.1]
Group 1 (pregnant women at risk of abortion without bleeding)	20	152.1 [146.2; 156.8]*	13.4 [12.5; 14.3]*	41.3 [39.0; 43.7]*

Notes: Kruskal–Wallis test: for chorion volume $H=14.2$, $p<0.001$; VI: $H=17.8$, $p<0.001$; FI: $H=15.6$, $p<0.001$. Post-hoc (Bonferroni-corrected data): differences between Control Group and Group I adjusted $p<0.01$ for all indicators.

Table 2. The condition of the chorion at the threat of miscarriage with bleeding at 10–13 weeks of gestation.

Examined groups	n	The volume of the chorion (Vx cm^3)	Vascularization index (VI)	Blood flow index (FI)
Control Group	20	164.0 [162.5; 165.2]	19.4 [18.3; 20.7]	49.2 [48.5; 50.1]
Group 2 (pregnant women at risk of abortion with bleeding)	22	131.5 [127.1; 135.9]**	9.6 [8.9; 10.4]**	34.1 [31.8; 36.3]**

Note: Kruskal–Wallis test: $H=28.4$, $p<0.001$ for all indicators. Post-hoc (Dunn and Bonferroni): differences between Control Group and Group 2 adjusted $p<0.001$, between Group 1 and Group 2 – $p<0.01$.

indicators of chorionic volume, vascularization index and blood flow index in the group with retrochorial hematoma compared to the threat group without bleeding (adjusted p<0.01 for all indicators according to Dunn's test with Bonferroni correction).

Discussion

Previously, we published a study [12] on the same patients, examining general aspects of the state of extraembryonic structures in threatened miscarriage in early pregnancy. In contrast to the previous work, the present study provides, for the first time, a quantitative comparison of chorionic vascularization indices between the groups with threatened miscarriage without bleeding and with retrochorial hematoma, and assesses the degree of their differences using nonparametric statistics with correction for multiple comparisons (Kruskal–Wallis test with Dunn's post-hoc test and Bonferroni correction).

The results of the investigation show that the threat of abortion at [10–13] weeks of gestation, especially in the presence of RCH, is accompanied by significant structural and functional changes in the chorion. In patients of Group 2 the median chorionic volume was reduced by 20.1% compared to controls (p<0.001), and the indices of VI and FI were reduced by 50.0% and 30.7%, respectively (p<0.001). Even in the absence of bleeding (Group 1), a significant decrease in these indicators was observed (p<0.01 relative to the Control Group), which confirms the negative effect of the increased tone of the myometrium without a hematoma.

The obtained data are consistent with modern ideas about the pathogenesis of miscarriage. Disruption of cytotrophoblast invasion and incomplete reconstruction of spiral arteries, which underlie the threat of miscarriage, directly affect the formation of the chorion and the subsequent formation of the placenta [1; 7; 10]. In our study, a decrease in VI and FI indicates not only hypoplasia of the chorion, but also insufficient angiogenesis, which creates prerequisites for chronic fetoplacental insufficiency in the 2nd and 3rd trimesters.

Of particular note is the fact that corporal CG, which are traditionally considered less prognostically dangerous, were still associated with the worst indicators of the chorion condition in our sample. This can be explained by the fact that the very presence of a hematoma, even without direct detachment of the fetal egg in the area of the internal eye, indicates deep disorders of utero-placental hemodynamics. Probably, the key role is played not so much by the location of the hematoma, but by the degree of dysfunction of the endometrial-chorionic complex, which is confirmed by a decrease in VI almost twice.

Comparing our results with the data of other authors [2; 3; 8], it should be noted that most studies focus on the clinical consequences of miscarriage (premature birth, pregnancy loss), while the morpho-functional state of the chorion at the end of the first trimester is insufficiently studied. Our advantage is the quantification of VI and FI using the VOCAL program, which allows us to objectify the degree of angiogenesis. At the same time, the small amount of samples (n=[20–22]) and the lack of long-term follow-up of these women in the 2nd–3rd trimesters limit the possibility of direct extrapolation of the obtained data to the risk of developing preeclampsia or fetal growth retardation.

The clinical significance of our results is that even under the conditions of successful preservation of pregnancy and cessation of bleeding (in 90.9% of patients of the Group 2, hemostasis was achieved for an average of 2.8 days), changes in the chorion remain stable for at least 13 weeks. This dictates the need for further monitoring of the condition of the fetus and the placenta, and not only for ascertaining the reduction of the hematoma. It can be assumed that these patients form a risk group for placental dysfunction later, even in the absence of obvious clinical manifestations in the first trimester.

Our study confirms that the threat of miscarriage at [10–13] weeks, especially with the formation of RCH, is not only an obstetric complication "here and now", but also a marker of impaired placentation with long-term consequences. Further prospective studies with larger samples and prenatal follow-up are needed to clarify the prognostic value of VI and FI in the early fetal period.

Conclusions

1. Retrochorial hematomas formed at the threat of miscarriage at [10–13] weeks of gestation are associated with hypoplasia of the chorion (reduction of the median chorionic volume by 20.1% compared to the control) and impaired maturation. In the threat of miscarriage without bleeding (Group 1), the chorionic volume decreased by 7.4%, the vascularization index by 30.9%, and the blood flow index by 16.1% relative to the control.

2. A decrease in the vascularization index and blood flow in the chorion creates a high risk of placental dysfunction, which in turn worsens the prognosis for the further course of pregnancy.

Funding and Acknowledgments

The research was conducted as a private initiative of the authors, did not receive funding from grant programs, and the research topic was not officially registered in the state register of scientific topics.

Declarations

Conflict of interest is absent. The author has given consent to the publication of the article under the terms of the Creative Commons Attribution-NonCommercial-Share Alike 4.0 International License and a public agreement with the publisher, to the processing and publication of their personal data.

The author of the manuscript states that in the process of conducting research, preparing, and editing this manuscript, no generative AI tools or services were used to perform any of the tasks listed in the Generative AI Delegation Taxonomy (GAIDeT, 2025). All stages of work (from the development of the research concept to the final editing) were carried out without the involvement of generative artificial intelligence, exclusively by the author.

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Received: 08 Sep 2025
Accepted: 29 Dec 2025
Published: 31 Dec 2025

Cite in Vancouver style as: Kravchenko OV. Threat of miscarriage at 10–13 weeks of gestation: Consequences and possible risks. Inter Collegas. 2025;12(4):40-5. https://doi.org/10.35339/ic.2025.12.4.kov

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