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Relationship between PAPP-A levels, placental morphometric parameters, and perinatal outcomes in pregnant women with fetoplacental insufficiency

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Fetal growth restriction (FGR) and fetoplacental insufficiency (FPI) are major complications of pregnancy associated with adverse perinatal outcomes. Pregnancy-associated plasma protein A (PAPP-A) and placental morphometry have been proposed as potential predictors of fetal growth and neonatal health.

Aim – to evaluate the relationship between first-trimester PAPP-A, placental morphometry, and neonatal outcomes in pregnancies complicated by FPI and FGR, and to assess their predictive value for monitoring intrauterine growth.

Materials and methods. A prospective cohort study was conducted between 2023 and 2025. The study included 42 deliveries from women aged 20–40 years with FPI and FGR. Maternal and neonatal data were collected. Placental morphometry and PAPP-A were analyzed for correlation with neonatal outcomes. Statistical analyses included mean ± standard deviations, ranges, 95% confidence intervals, t-tests, analysis of variance (ANOVA), and Pearson/Spearman correlation coefficients.

Results. Gestational age ranged from 30^{+4} to 40^{+6} weeks. Preterm deliveries (<37 weeks) were less frequent and associated with lower birth weight (LBW) and Apgar scores. The mean birth weight was 3280±417 g, mean neonatal length 50.8±2.9 cm, mean placental volume 70.9±36.5 cm³, and mean PAPP-A 0.92±0.70 MoM. Reduced PAPP-A (<0.5 MoM) was associated with LBW (<2900 g) and smaller placental volume, whereas elevated PAPP-A (>1.5 MoM) corresponded to higher birth weight (>3700 g) and larger placental volume. PAPP-A positively correlated with birth weight and placental volume. Increased placental volume was also associated with greater neonatal length and mass.

Conclusion. PAPP-A levels and placental morphometric characteristics are significant predictors of fetal growth and neonatal outcomes in pregnancies complicated by FPI and FGR.

The research was carried out in accordance with the principles of the Declaration of Helsinki. The informed consent of the patients was obtained for conducting the studies.

The author declares the absence of conflict of interests.

Keywords: pregnancy-associated plasma protein A (PAPP-A), placental volume, fetal growth restriction, fetoplacental insufficiency, neonatal outcomes.

Взаємозв'язки між рівнями PAPP-A, морфометричними параметрами плаценти та перинатальними наслідками у вагітних жінок з фетоплацентарною недостатністю

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Затримка росту плода (ЗРП) та фетоплацентарна недостатність (ФПН) є основними ускладненнями вагітності, пов'язаними з несприятливими перинатальними результатами. Плазмовий протеїн А, пов'язаний із вагітністю (PAPP-A), та морфометрія плаценти були запропоновані як потенційні предиктори росту плода та здоров'я новонародженого.

Мета – оцінити зв'язок між PAPP-A у першому триместрі, морфометрією плаценти та неонатальними результатами під час вагітності, ускладненій ЗРП та ФПН, та оцінити їхню прогностичну цінність для моніторингу внутрішньоутробного росту.

Матеріали та методи. Проспективне когортне дослідження було проведено у 2023–2025 рр. Дослідження охопило 42 жінок віком 20–40 років із ЗРП та ФПН під час пологів. Зібрано дані про матерів та новонароджених. Морфометрію плаценти та PAPP-A аналізували щодо кореляції з неонатальними результатами. Статистичний аналіз охопив середнє значення ± стандартне відхилення, діапазони, 95% довірчі інтервали, t-тести, дисперсійний аналіз (ANOVA) та коефіцієнти кореляції Пірсона/Спірмена.

Результати. Гестаційний вік коливався від 30^{+4} до 40^{+6} тижнів. Передчасні пологи (<37 тижнів) були рідшими та пов'язані з нижчою вагою під час народження та балами за шкалою Апгар. Середня вага під час народження становила 3280±417 г, середня довжина новонародженого 50,8±2,9 см, середній об'єм плаценти 70,9±36,5 см³, а середній PAPP-A 0,92±0,70 MoM. Знижений рівень PAPP-A (<0,5 MoM) пов'язаний із меншою вагою під час народження (<2900 г) та меншим об'ємом плаценти, тоді як підвищений рівень PAPP-A (>1,5 MoM) відповідав вищій вазі під час народження (>3700 г) та більшому об'єму плаценти. PAPP-A позитивно корелював з вагою під час народження та об'ємом плаценти. Збільшений об'єм плаценти також пов'язаний із більшою довжиною та масою новонародженого.

Висновок. Рівні PAPP-A та морфометричні характеристики плаценти є значними предикторами росту плода та неонатальних результатів під час вагітності, ускладненій ФПН та ЗРП.

Дослідження виконано відповідно до принципів Гельсінської декларації. На проведення досліджень отримано інформовану згоду пацієнток.

Автор заявляє про відсутність конфлікту інтересів.

Ключові слова: плазматичний протеїн А, пов'язаний із вагітністю (PAPP-A), об'єм плаценти, затримка росту плода, фетоплацентарна недостатність, неонатальні результати.

Fetal growth restriction (FGR) is one of the most common complications of pregnancy and is associated with an increased risk of adverse perinatal outcomes. FGR is linked to a significantly higher risk of perinatal mortality, low birth weight, neurological impairments, as well as long-term metabolic disorders that may manifest in childhood and adulthood. Timely identification of pregnant women at high risk of FGR remains a key challenge in modern perinatal medicine, enabling the implementation of preventive and therapeutic interventions at early stages of pregnancy. A particular challenge lies in differentiating between a constitutionally small fetus, which develops within its genetic potential, and a pathologically small fetus, whose growth is restricted due to an underlying maternal, placental, or fetal pathology [8,10,11].

Fetoplacental insufficiency (FPI) is a key factor in the development of FGR. Structural and functional abnormalities of the placenta lead to a reduced supply of oxygen and nutrients from the mother to the fetus, directly affecting fetal weight and growth. Therefore, both placental morphometric parameters and biochemical markers reflecting its functional status are of significant importance [12].

A key biomarker is pregnancy-associated plasma protein A (PAPP-A), a protein produced by the trophoblast that plays a role in the regulation of insulin-like growth factors and placental angiogenesis. PAPP-A is an important pregnancy biomarker for the early detection of complications, including FGR [1,7].

The volume and functional status of the placenta reflect the mother's ability to supply nutrients to the fetus, and their relationship with neonatal parameters helps predict perinatal outcomes and improve pregnancy monitoring. Low first-trimester PAPP-A levels are associated with an increased risk of fetal growth restriction, preeclampsia, and preterm birth. Additionally, placental morphometric parameters such as weight, volume, and chorionic villi surface area reflect the organ's capacity to support normal intrauterine fetal growth [2,4–6].

Despite numerous studies, the combined interaction of biochemical markers and placental morphometric characteristics in assessing the risk of FGR and predicting newborn weight and length remains insufficiently explored [3,9].

Therefore, an important objective is to investigate the relationship between PAPP-A levels, placental morphometric parameters, and perinatal outcomes in pregnant women with FPI.

The aim of this study was to determine the prognostic value of PAPP-A levels and placental morphometric parameters for the early identification of FGR risk and the assessment of newborn outcomes.

Material and methods of the study

Study design and setting. A prospective cohort study was conducted from 2023 to 2025 at the Department of Obstetrics and Gynecology II of Azerbaijan Medical University (AMU) and at the laboratory of the Educational Surgical Clinic of AMU.

Study population. The study included data from 42 deliveries. The parameters assessed were fetal weight (g), gestational age (weeks and days), placental volume (cmi), PAPP-A levels (MoM), Apgar scores, and newborn length (cm). Of the 42 deliveries included in the study, complete PAPP-A data were available for 36 cases, and complete paired datasets for correlation analyses in 30 cases. Apgar score analysis included 41 liveborn newborns, as one pregnancy resulted in intrauterine fetal demise.

For analysis, mean values, ranges, and correlation coefficients between PAPP-A levels, placental volume, and neonatal physical parameters were calculated. PAPP-A values were interpreted according to reference ranges: <0.5 MoM was considered low, 0.5–1.5 MoM was normal, and >1.5 MoM was high.

Inclusion and exclusion criteria. The study included pregnant women aged 20–40 years with FPI and FGR who provided written informed consent to participate. Exclusion criteria comprised women with malignant neoplasms, chronic kidney disease, stage III arterial hypertension, as well as pregnant women younger than 20 or older than 40 years, or those who declined participation in the study.

Clinical and functional methods. Data were collected on maternal history, course of pregnancy, complications, and the condition of the newborn.

Ultrasound examinations and Doppler studies were performed to assess the pulsatility index (PI) of the uterine and umbilical arteries, the fetal middle cerebral artery, and to calculate the cerebroplacental ratio (CPR). Measurements were taken when the fetus was at rest, with three consecutive readings recorded and averaged. Reference values were based on the International Society of Ultrasound in Obstetrics and Gynecology

(ISUOG, 2023) guidelines: uterine artery PI 0.8–1.4, umbilical artery PI 0.6–0.9, and CPR >1.08.

Laboratory methods. PAPP-A levels were measured during first-trimester screening and converted to MoM for standardization. Additionally, key neonatal biochemical parameters were recorded, including lactate, glucose, malondialdehyde (MDA), and proteins C and S.

Morphological assessment of the placenta. Immediately after delivery, placental weight and the area of chorionic villi were measured, and dystrophic changes were assessed histologically. The protocol followed the standards of the European Society of Placental Pathology (ESPR, 2022).

Perinatal outcomes of newborns. The newborns' birth weight and length, head and abdominal circumference, and Apgar scores at 1 and 5 minutes were systematically recorded, along with key biochemical markers. These data were used to assess the impact of PAPP-A levels and placental volume on neonatal status.

Statistical analysis. All data were processed using SPSS v.25.0. Continuous variables are presented as mean ± SD (M±SD) and 95% confidence intervals (CI), while categorical variables are expressed as absolute numbers and percentages. Group comparisons were performed using Student's t-test, analysis of variance (ANOVA), and non-parametric tests as appropriate. Correlations were assessed with Pearson's and Spearman's coefficients. Statistical significance was set at $p<0.05$.

Ethical considerations. The study was conducted in accordance with the Declaration of Helsinki (2013) and was approved by the local Ethics Committee of AMU. All participants provided written informed consent to participate.

Study limitations. The main limitations of this study include the relatively small sample size and the absence of certain laboratory measurements in some participants. Additionally, the study was conducted at a single medical center, which may limit the generalizability of the findings to a broader population.

Results of the study and discussion

In the study group, gestational age ranged from 30 weeks and 4 days to 40 weeks and 6 days. For analytical purposes, deliveries were classified as preterm (<37 weeks) and term (37–41 weeks). Preterm births were relatively infrequent in this cohort and were generally associated with lower birth weights (LBW) and lower Apgar scores compared to term newborns.

During the analysis, data were collected on neonatal birth weight and length, gestational age, placental volume, PAPP-A levels (MoM), and Apgar scores. The means, standard deviations, ranges, and 95% CI for these parameters are presented in Table 1.

The mean birth weight was 3280±417 g, with a 95% CI of 3154–3406 g and a range of 2270–4190 g. The mean length of the newborns was 50.8±2.9 cm, with a 95% CI of 49.9–51.7 cm and a range of 44–56 cm.

Placental volume showed considerable variability, ranging from 26 to 147 cm^3, with a mean of 70.9±36.5 cm^3 and a 95% CI of 59.9–81.9 cm^3. PAPP-A levels ranged from 0.27 to 3.25 MoM, with a mean of 0.92±0.70 and a 95% CI of 0.71–1.13 MoM, reflecting the distribution of this biochemical marker in the study group.

Apgar scores of the newborns ranged from 5 to 9, with a mean of 7.8±0.6 and a 95% CI of 7.62–7.98, indicating generally satisfactory neonatal condition. The inclusion of 95% CI allows for the assessment of the precision of the mean values and provides a basis for subsequent analysis of the relationships between PAPP-A levels, placental characteristics, and neonatal parameters.

Most pregnant women had PAPP-A levels within the reference range. Reduced PAPP-A levels (<0.5 MoM) were observed in some patients and were more frequently associated with lower fe-

Table 1

Key characteristics of newborns and pregnancy parameters

Parameter	Mean ± SD	95% CI	Range
Birth weight, g	3280±417	3154–3406	2270–4190
Birth length, cm	50.8±2.9	49.9–51.7	44–56
Gestational age	38 weeks 4 days	–	30 weeks 4 days – 40 weeks 6 days
Placental volume, cm^3	70.9±36.5	59.9–81.9	26–147
PAPP-A, MoM	0.92±0.70	0.71–1.13	0.27–3.25
Apgar score	7.8±0.6	7.62–7.98	5–9

Table 2

Distribution of cases by PAPP-A categories and corresponding percentage of the total sample

PAPP-A category	Number of cases	%
< 0.5 MoM	9	25
0.5 – 2.0 MoM	23	63.9
> 2.0 MoM	4	11.1
Total	**36**	**100**

tal weight and smaller placental volume. Elevated PAPP-A levels (>2.0 MoM) were significantly less common and were generally accompanied by higher fetal weight and larger placental volume (Table 2).

Data analysis revealed that PAPP-A MoM levels were significantly positively correlated with neonatal birth weight (r=0.42, p<0.01), indicating a direct relationship between the concentration of this protein and fetal growth in utero. In particular, among pregnant women with reduced PAPP-A levels (<0.5 MoM), newborn birth weight was below 2900 g, whereas higher PAPP-A values (>1.5 MoM) were observed in infants with birth weights exceeding 3700 g, confirming the role of PAPP-A as a marker of intrauterine growth (Figure 1).

At the same time, a positive, although less pronounced, correlation was found between placental volume and neonatal length (r=0.36, p<0.05). Newborns delivered by women with larger placental volumes demonstrated greater birth length, reflecting the importance of placental morphometric characteristics in predicting fetal physical development (Figure 2).

For a clearer presentation of these data, Table 3 was constructed, showing the mean values of neonatal birth weight and length according to PAPP-A level categories (Table 3).

The analysis of Table 2 demonstrates a clear relationship: as PAPP-A levels increase, the mean

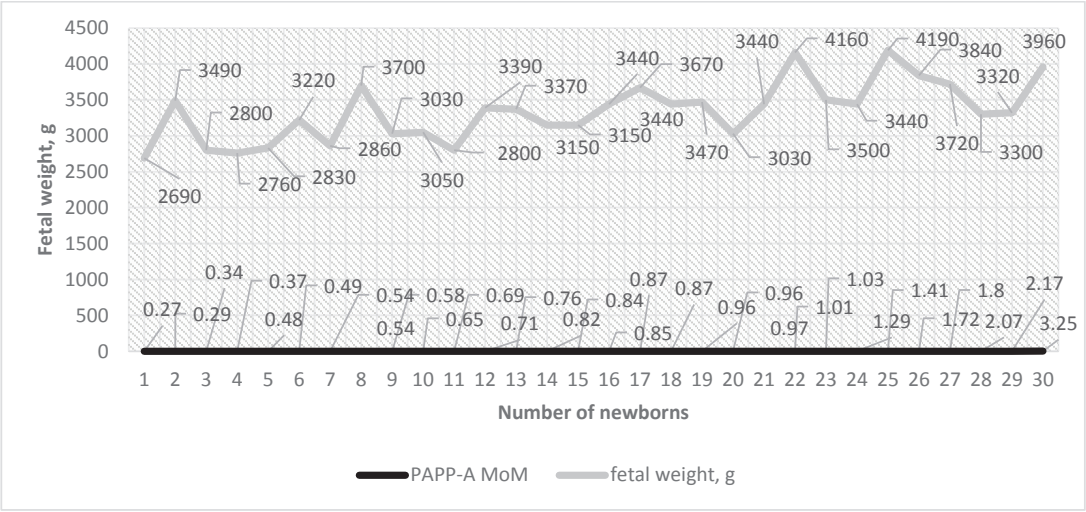

Fig. 1. Correlation between PAPP-A (MoM) and birth weight (g) in newborns

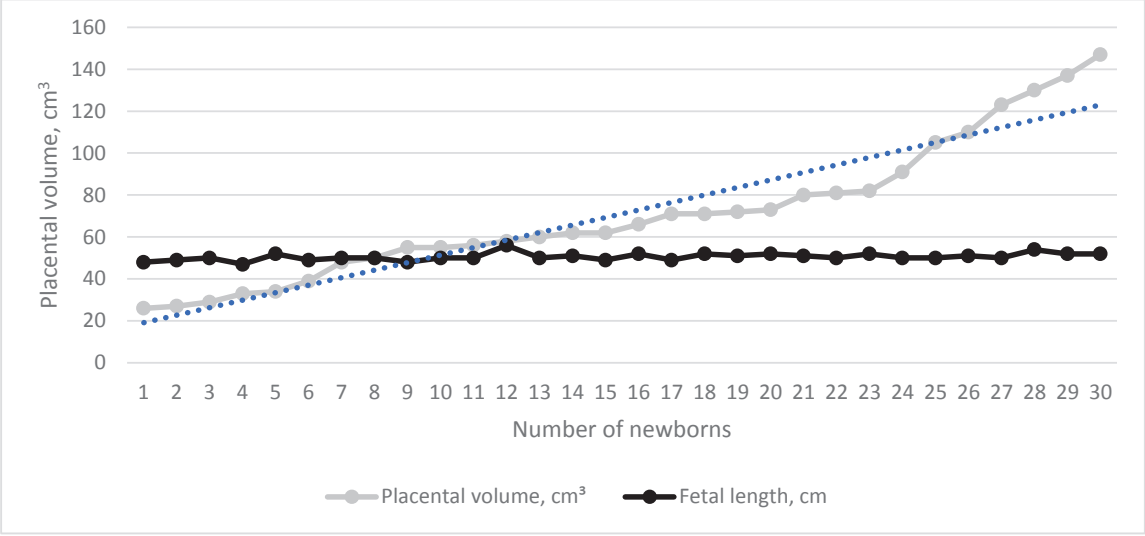

Fig. 2. Correlation between placental volume and fetal length in newborns with FGR and placental insufficiency

Table 3

Influence of PAPP-A levels on neonatal birth weight and length

PAPP-A (MoM) category	Number of newborns	Mean birth weight, g (M±SD)	95% CI (weight)	Mean length, cm (M±SD)	95% CI (length)
<0.5 (low)	9	2765±120	2635–2895	49.0±2.1	47.0–51.0
0.5–1.5 (normal)	23	3260±310	3160–3360	50.5±2.7	49.7–51.3
>1.5 (high)	4	3810±220	3660–3960	52.0±2.3	50.9–53.1

birth weight and length of newborns also increase. These findings highlight the clinical importance of monitoring PAPP-A levels in predicting intrauterine fetal development and support its use in combination with placental morphometric parameters to assess the risk of FGR.

For a more detailed analysis of the relationship between PAPP-A levels, placental morphometric parameters, and fetal weight, all newborns were divided into three groups according to birth weight: less than 3000 g, 3000–3500 g, and more than 3500 g (Figure 3).

The analysis demonstrated a clear relationship between fetal weight, mean PAPP-A levels, and placental volume. Infants with a birth weight of less than 3000 g had lower PAPP-A levels (0.43 MoM) and a smaller mean placental volume (53 cm^3), reflecting a potential association between low PAPP-A and restricted intrauterine growth. In the group with birth weights of 3000–3500 g, the mean PAPP-A level was 0.85 MoM, while the mean placental volume increased to 71 cm^3, corresponding to normal growth parameters. Newborns with birth weights above 3500 g showed higher PAPP-A values (1.45 MoM) and larger placental volumes (87 cm^3), confirming the positive influence of these factors on fetal growth.

The analysis of Table 2 demonstrates a clear trend: as fetal weight increases, the mean values of PAPP-A and placental volume also increase. These findings highlight the role of PAPP-A and placental morphometry as important indicators for assessing intrauterine development and predicting neonatal outcomes.

During the study, one case of intrauterine fetal demise was recorded. This case was characterized by low fetal weight and a relatively small placental volume, which may indicate severe placental dysfunction.

The condition of the newborns at birth was assessed using the Apgar score. In the study, the values ranged from 5 to 9 points, with a mean score of 7.8±0.6. Most newborns were in satisfactory condition at birth, as evidenced by the predominance of Apgar scores of 7–8. In several cases, lower scores were observed, which may have been associated with preterm birth or signs of placental insufficiency (Figure 4).

The distribution of Apgar scores showed that most newborns were in satisfactory condition at birth. The most frequently observed scores were 7 and 8, recorded in 23 and 16 newborns, respectively. One newborn had a score of 5, while the maximum score of 9 was observed in one case. Apgar score analysis was restricted to 41 liveborn newborns, as one case was complicated by intrauterine fetal demise and was therefore not eligible for postnatal assessment.

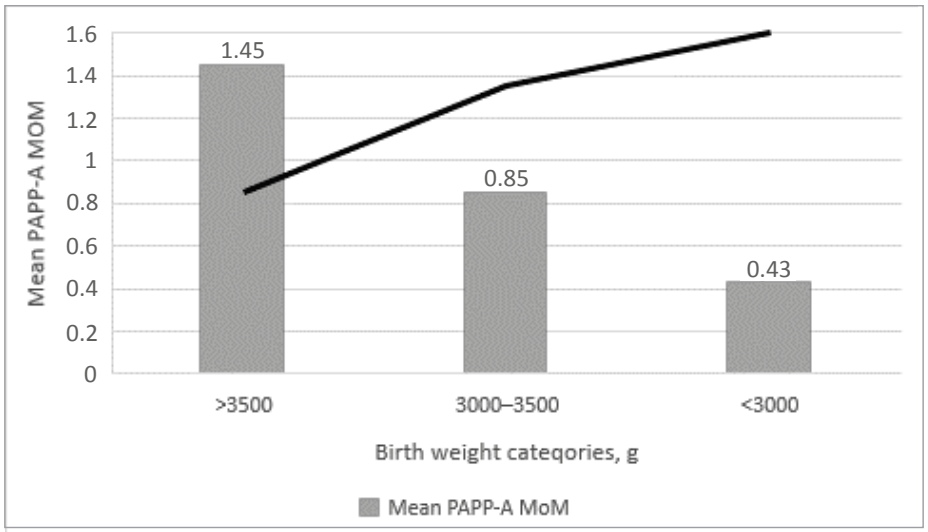

Fig. 3. Mean PAPP-A (MoM) and placental volume according to birth weight categories

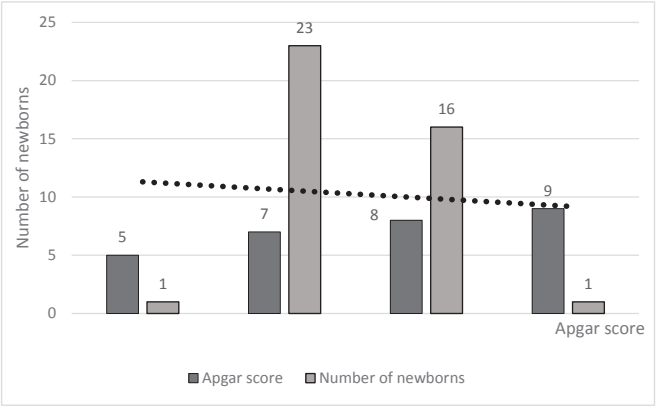

Fig.4. Distribution of Apgar scores among newborns in the study group

The distribution of birth weights showed that the largest proportion of newborns had a weight in the range of 3000–3500 g. Low birth weight (<2500 g) was observed in 3 cases. Eleven newborns had a birth weight of 2500–3000 g. Higher birth weights (3500–4000 g) were recorded in 7 newborns, while birth weights above 4000 g were observed in 4 cases (Figure 5).

A positive correlation was observed between placental volume and birth weight. As placental volume increased, there was a corresponding tendency for higher fetal weight. These findings underscore the important role of placental development in supporting normal intrauterine fetal growth.

Analysis of morphometric data showed that newborns with a reduced placental volume (<50 cm^3, n=9) had a mean birth weight of 2760±320 g. For those with a normal placental volume (50–100 cm^3, n=21), the mean birth weight was higher at 3320±280 g. Newborns with an increased placental volume (>100 cm^3, n=6) had a mean birth weight of 3710±310 g.

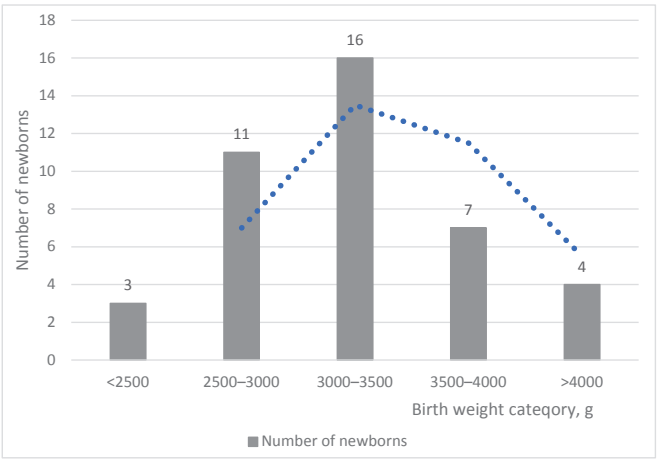

Fig.5. Distribution of birth weight among newborns in the study group

These results confirm a direct relationship between placental volume and fetal weight and highlight its role in supporting normal intrauterine growth.

The obtained results confirm the important role of placental factors and biochemical markers in the formation of fetal intrauterine growth. In this study, a positive correlation was identified between the level of PAPP-A and fetal birth weight, which is consistent with the findings of several international studies [1,7,11,12].

It is known that PAPP-A is an important protein produced by the trophoblast and plays a significant role in placental development, angiogenesis, and the regulation of insulin-like growth factors. A decreased level of this marker in the first trimester of pregnancy is often considered one of the early signs of placental dysfunction. The analysis showed that lower PAPP-A levels were more frequently observed in newborns with LBW, whereas higher levels of this marker were associated with greater fetal mass. These findings are consistent with previous studies, which indicate that decreased PAPP-A levels may be linked to an increased risk of FGR and placental insufficiency [7,12].

Furthermore, the study revealed a positive correlation between placental volume and fetal mass. The placenta is a key organ responsible for transporting oxygen and nutrients from the mother to the fetus. A reduction in placental size or functional activity can lead to impaired intrauterine fetal growth.

The results indicate that an increase in placental volume is associated with a tendency toward higher neonatal birth weight, underscoring the importance of placental morphological characteristics in ensuring normal pregnancy outcomes.

A positive correlation was also observed between PAPP-A levels and placental volume, suggesting that this biochemical marker may reflect the processes of placental development and functional status. Several studies indicate that decreased PAPP-A levels may be associated with impaired implantation and the development of placental insufficiency, which can subsequently lead to adverse perinatal outcomes [1,2,4,6].

Particular attention should be paid to the observed relationship between gestational age and fetal weight. The data demonstrate a consistent increase in fetal body mass as pregnancy progresses, reflecting the physiological mechanisms of intrauterine development. Thus, the results of

this study underscore the importance of a comprehensive assessment of both biochemical and morphometric placental indicators for predicting intrauterine fetal growth and perinatal outcomes. Measuring PAPP-A levels in combination with an analysis of placental morphometric characteristics can be regarded as a valuable diagnostic tool for the early identification of risks associated with fetoplacental dysfunction. At the same time, it should be noted that this study has certain limitations. The sample size was relatively small, and some parameters were missing in individual cases. Moreover, the research was conducted at a single clinical center. Future studies with larger sample sizes are needed to confirm these findings and to more thoroughly investigate the role of placental factors in shaping intrauterine fetal growth.

Conclusions

In the study group of pregnant women with FGR and FPI, the analysis revealed significant associations between placental biochemical and morphometric parameters and perinatal outcomes.

It was found that PAPP-A levels positively correlate with fetal weight, with low values (<0.5 MoM) being associated with a birth weight below 2900 g. A positive relationship was also observed between placental volume and both birth weight and length, confirming the importance of placental morphological characteristics for normal intrauterine development. The positive correlation between PAPP-A and placental volume indicates the role of this marker in assessing placental functional status.

The obtained data emphasize the importance of comprehensive pregnancy monitoring, including the assessment of PAPP-A levels, placental morphometric parameters, and fetal condition, for the early identification of intrauterine growth restriction risk and the optimization of perinatal care.

The results of this study may serve as a basis for further large-scale research aimed at clarifying the prognostic value of PAPP-A and placental morphometric characteristics in pregnancy monitoring and complication prevention.

The author declares the absence of conflict of interests.

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