

# Obstetrical and perinatal consequences of childbirth in women with antenatally undiagnosed fetal growth restriction

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Fetal growth restriction (FGR) is one of the most studied topics in the medicine of the mother and fetus. However, not identified antenatally FGR can have an increased risk of both perinatal morbidity and mortality, as well as adverse long-term consequences. The identification of FGR during pregnancy will contribute to the reduction of both perinatal morbidity and perinatal mortality.

**Aim.** Based on a retrospective analysis, assess the obstetric and perinatal consequences of childbirth in women with antenatally undiagnosed fetal growth restriction.

**Materials and methods.** An analysis of 488 cases of childbirth in women with singleton pregnancy, who gave birth to a live child, was conducted. In all cases, the gestational age was  $\geq 22$  weeks with a fetal weight less than the 10<sup>th</sup> percentile for the corresponding gestational age. Depending on the antenatally established diagnosis of FGR, two study groups were formed: group I consisted of 204 (41.8 %) cases with antenatally diagnosed FGR, group II – 284 (58.2 %) cases in which signs of FGR were identified after the birth of the child. Maternal characteristics, neonatal outcomes, and evaluation of short-term infant outcomes were analyzed.

**Results.** Both groups were dominated by women with first births, the number of which was almost the same. Somatic pathology was almost 2 times more common in women of group I, 17.2 %, compared to 9.2 % of women in group II ( $p < 0.01$ ), this indicates that the majority of women who were not diagnosed with FGR during pregnancy belong to the low-risk group. Fetuses with impaired blood flow in the umbilical cord arteries were twice as common in group I, 49.5 % versus 23.9 % in group II ( $p < 0.0001$ ), and the frequency of absent/reversible end flow in the umbilical arteries in group I compared to group II, prevailed 3 times ( $p < 0.0001$ ), indicating more serious lesions of the placenta and, as a result, early manifestation of the fetal condition disorder. The frequency of premature abdominal delivery was 3.75 times higher in group I compared to group II. The most frequent indication for cesarean delivery in both groups was signs of fetal distress syndrome. Analysis of neonatal outcomes showed that the average birth weight was significantly lower in group I and was  $2180 \pm 55$  g against  $2420 \pm 61$  g in group II ( $p < 0.0001$ ). The need for hospitalization of newborns in the intensive care unit had no statistical difference between the groups ( $p > 0.05$ ). However, the complications of the early neonatal period and the total length of stay in the hospital were greater in children of the I group, compared to the II group ( $p < 0.0001$ ).

**Conclusions.** The results of the conducted research indicate a low level of prenatal diagnosis of fetal growth restriction. Most pregnant women with antenatally undiagnosed fetal growth restriction belong to the group of low perinatal risk. The most frequent indication for cesarean section operation, regardless of the date of delivery, in both groups were signs of fetal distress, the frequency of which was 1.5 times higher in the antenatally diagnosed fetal growth retardation group. Newborns with an undetected growth anomaly before delivery have an increased risk of fetal distress, the severity of which is determined by the degree of deterioration of fetal oxygenation, and not by weight percentile, which requires more careful observation of fetuses with signs of growth restriction.

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## Акушерські та перинатальні наслідки пологів у жінок з антенатально не діагностованою затримкою росту плода

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Затримка росту плода (ЗРП) – одна з найкраще вивчених тем у медицині матері та плода. Але не ідентифікована антенатально ЗРП спричиняє підвищений ризик перинатальної захворюваності та смертності, а також несприятливі віддалені наслідки. Виявлення ЗРП під час вагітності сприятиме зниженню перинатальної і захворюваності, й смертності.

**Мета роботи** – на підставі ретроспективного аналізу здійснити оцінювання акушерських і перинатальних наслідків розродження жінок з антенатально не діагностованою затримкою росту плода.

**Матеріали та методи.** Проаналізували 488 випадків пологів у жінок з одноплідною вагітністю, які народили живу дитину. В усіх випадках термін вагітності становив  $\geq 22$  тижні з масою плода, що менша за 10

перцентиль для відповідного терміну гестації. Залежно від антенатально встановленого діагнозу ЗРП, сформували дві групи дослідження: I – 204 (41,8 %) випадки з антенатально діагностованою ЗРП; II – 284 (58,2 %) випадки, коли ознаки ЗРП ідентифіковано після народження дитини. Вивчили материнські характеристики, неонатальні результати, оцінили короткострокові результати лікування немовлят.

**Результати.** В обох групах переважали жінки з першими пологами, кількість яких в групах зрівняна. Соматичну патологію майже вдвічі частіше діагностували в жінок I групи (17,2 %) порівняно з II (9,2 %) ( $p < 0,01$ ). Це свідчить, що більшість жінок, у яких під час вагітності не було діагностовано ЗРП, належать до групи низького ризику. Порушення кровотоку в артеріях пуповини вдвічі частіше фіксували в плодів I групи (49,5 %) щодо II (23,9 %) ( $p < 0,0001$ ). Частота нульового / реверсивного кровотоку в артеріях пуповини втричі переважала в I групі порівняно з II ( $p < 0,0001$ ). Це свідчило про складніші ураження плаценти, а отже й ранню маніфестацію порушення стану плода. Частота дострокового абдомінального розродження в 3,75 раза вища в I групі. Найчастіше показання до кесаревого розтину в обох групах – ознаки дистрес синдрому плода. Аналіз неонатальних наслідків показав: середня маса при народженні вірогідно менша в I групі, становить  $2180 \pm 55$  г, у II –  $2420 \pm 61$  г ( $p < 0,0001$ ). Не виявили статистично значущої різниці між групами за необхідністю госпіталізації новонароджених у відділення інтенсивної терапії ( $p > 0,05$ ). Втім, частота ускладнень раннього неонатального періоду та загальна тривалість перебування в стаціонарі більші в дітей I групи порівняно II ( $p < 0,0001$ ).

**Висновки.** Результати дослідження свідчать про низький рівень допологової діагностики затримки росту плода. Більшість вагітних з антенатально не діагностованою затримкою росту плода належать до групи низького перинатального ризику. Найчастіше показання до операції кесаревого розтину (незалежно від терміну розродження) в обох групах – ознаки дистресу плода, частота якого в 1,5 раза більша в групі антенатально діагностованої затримки росту плода. Новонароджені з не виявленою перед пологами аномалією росту мають підвищений ризик дистресу плода, тяжкість якого визначається ступенем погіршення оксигенації, а не процентилем маси. Це зумовлює необхідність ретельнішого спостереження за плодами з ознаками затримки росту.

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Fetal growth restriction (FGR) is one of the most studied topics in the medicine of the mother and fetus. This is due not only to the relationship between the FGR and the postnatal consequences for the newborn but also to unresolved issues concerning the diagnosis and treatment of this pathology [1,2]. Over the past 40 years, a considerable amount of evidence has been obtained to clarify the clinical condition of the fetus with a suspected FGR and the role of fetal care parameters, both for predicting the clinical course and evaluating its condition during observation. However, there are significant differences in the recommended guidelines for fetus management with suspected FGR [3,4,5]. Today, there are still some differences both in diagnostic criteria and in the tactics of management. FGR is a complex problem of modern obstetrics that the American College of Obstetricians and Gynaecologists (ACOG 2021) considers “the most relevant and difficult problem of modern obstetrics” [6]. Despite the various causes of FGR, it is a pathological condition that occurs because of placental vascular disorders, namely chronic oxygen deficiency and nutrients for the fetus due to impaired fetal-mother circulation [7,8,9].

Despite extensive studies, and public health policy aimed at reducing the number of infants with low body weight, the prevalence of FGR remains unacceptably high [10]. At the same time, not identified antenatally FGR can have an increased risk of both perinatal morbidity and mortality, as well as adverse long-term consequences of the cardiovascular system, and cognitive disorders in adulthood [11,12]. Also, the FGR is associated with 12 % mortality in antenatal and 8 % in neonatal periods [13].

One of the attempts to improve the prevention of stillbirth is the best detection of FGR during pregnancy. However, the monitoring of fetal growth is an insurmountable obstacle to

prenatal observation [4,5,6]. Despite the consensus on the importance of screening, the current practice of pregnancy monitoring is heterogeneous and antenatally from 10 % to 36 % of infants with weight at birth <10 percentile [14,15]. Therefore, the diagnosis of FGR during pregnancy and the optimization of delivery dates contribute to the reduction of both perinatal morbidity and perinatal mortality [16,17].

## Aim

Based on a retrospective analysis, assess the obstetric and perinatal consequences of childbirth in women with antenatally undiagnosed fetal growth restriction.

## Materials and methods

An analysis of 488 cases of childbirth in women with a singleton pregnancy who gave birth to a living baby from 2018 to 2021 in Zaporizhzhia was done. In all cases, pregnancy was  $\geq 22$  weeks with a fetus weight less than the 10<sup>th</sup> percentile for the appropriate gestation period. FGR was determined by the criteria for diagnosis of according to the current order of the Ministry of Health of Ukraine dated 02.10.2023 No. 1718 and guidelines of the European Society of Ultrasound in Obstetrics and Gynecology (ISUOG) [18,19]. The estimated weight of the fetus was designed by the formula of the Hodlock (HC-AC-FL). For interpretation of the percentage of newborn weight, reference data from the INTERGROWTH-21<sup>st</sup> was used [20].

Growth restriction in newborns was defined according to the criteria of the Consensus Definition (2018), which includes: birth weight of the child <3<sup>rd</sup> percentile, or a combination of

**Table 1.** Maternal characteristics in the studied groups

Indexes	I group, n = 204	II group, n = 284	p
Average pre-pregnancy weight, kg	61.1 ± 9.7	58.2 ± 11.0	0.0310
BMI	21.9 ± 2.8	20.6 ± 2.7	<0.0001
Parity			
1 childbirth	51.9 %	59.2 %	0.1144
Extragenital pathology	17.2 %	9.2 %	0.0083

three criteria: birth weight <10<sup>th</sup> percentile; head circumference <10<sup>th</sup> percentile; prenatal diagnosis of FGR; prenatal risk factors associated with FGR [21].

Following the aim of the study, depending on the antenatally established diagnosis of FGR, two study groups were formed: group I consisted of 204 (41.8 %) cases with antenatally diagnosed FGR, II group – 284 (58.2 %) cases with signs of FGR identified after the birth of the child. The average age of pregnant women was 28.1 ± 3.1 in group I and 29.5 ± 2.4 years in group II. The study analyzed maternal characteristics, weight gain during pregnancy, and the onset of any obstetric complications. Dates and method of delivery, birth weight of infants, and Apgar score at 1 and 5 minutes after birth were collected and recorded [22]. Also, an evaluation of the short-term results of the treatment of infants was carried out, namely: the need for hospitalization in the neonatal intensive care unit, artificial ventilation of the lungs for more than 24 hours, and the main neonatal complications (respiratory distress syndrome (RDS) of the newborn, necrotizing enterocolitis (NEC), intraventricular hemorrhage (IVH)), sepsis, accesses, and days of hospitalization in neonatal intensive care unit).

The research was conducted by the modern requirements of moral and ethical norms regarding the rules of ICH/GCP, the Declaration of Helsinki (1964), the Conference of the Council of Europe on Human Rights and Biomedicine, as well as the provisions of legislative acts of Ukraine.

Statistical processing of the results was conducted using licensed standard packages of multivariate statistical analysis application programs Statistica for Windows 13 (StatSoft Inc., No. JPZ804I382130ARCN10-J). Data are presented as M ± SD (mean ± standard deviation) or n (%). Testing of the hypothesis about the presence of discrepancies was conducted using the Student's test. Differences were considered statistically significant at p < 0.05. The correlation between the term of pregnancy and manifestations of distress of fetuses of different groups was evaluated by the Pearson correlation coefficient.

## Results

The analysis of maternal characteristics showed that the average pregnancy weight and body mass index (BMI) of women of group I were significantly higher compared to women of group II (p < 0.001) (Table 1).

The number of women with their first birth in both groups was almost the same: 51.9 % (106/204) in group I, against 59.2 % (168/284) in group II (p > 0.05). Somatic pathology was almost

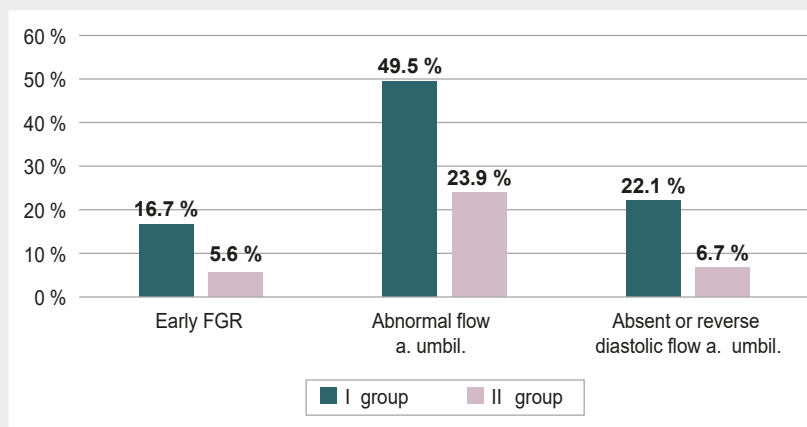
2 times more common in women of group I, 17.2 % (35/204), compared to 9.2 % (26/284) of women in group II (p < 0.01). Hypertensive disorders during pregnancy predominated among somatic pathologies, the frequency of which was 3.5 times higher in group I, 19.6 % (40/204) compared to 5.6 % (16/284) in group II.

Characterizing the condition of the fetus during pregnancy (Fig. 1), it should be noted that in both groups there was a predominance of fetuses with a late form of FGR, however, in group I the frequency in the early form of FGR was 3.5 times higher compared to group II (p < 0.0001). Fetuses with impaired blood flow in the arteries of the umbilical cord (pulsatility index (PI) > 95 %) were twice as common in group I versus in group II (p < 0.0001), and the frequency of absent end-diastolic flow in the umbilical arteries in group I compared to group II prevailed 3 times (p < 0.0001).

Peculiarities of the course of labour in the study groups showed that the average term of labour was significantly shorter in group I and was 37.4 ± 2.6 weeks against 38.2 ± 2.1 weeks in group II (p = 0.0004). The frequency of premature birth in both groups had no statistical difference, and in group I was 5.9 % (12/204) against 6.0 % (17/284) in group II (p = 0.1376). However, the frequency of preterm abdominal delivery was 3.75 times higher in group I compared to group II, 22.5 % (46/204) and 6.0 % (17/284), respectively (p < 0.0001). The percentage of cesarean sections prevailed in women of the I group, 52.0 % (106/204) compared to group II, 38.4 % (109/284) (p = 0.0029).

The most frequent indication for cesarean section in both groups were signs of fetal distress syndrome, however, in women of the I group, this indicator was 43.6 % (89/204), and in group II, respectively, 23.2 % (66/284) (p = 0.0014). It should be noted that a positive correlation of moderate strength was established between the term of pregnancy and manifestations of fetal distress in group I (r = 0.318) (p < 0.001), in contrast to group II, where the corresponding correlation was absent (r = 0.125) (p > 0.05). The frequency of vacuum extraction of the fetus was higher in women of group II, 4.9 % (14/284), against 1.5 % (3/204), respectively, in group I (p = 0.041). The frequency of placental abruption was not significantly different between the groups and was 0.5 % (1/204) in the I and 2.1 % (6/284) in group II (p = 0.1422).

Analysis of neonatal outcomes showed that the average birth weight was significantly lower in group I and was 2180 ± 55 g against 2420 ± 61 g in group II (p < 0.0001). It should be noted that the proportion of newborns weighing up to 1000.0 and 1000–2000.0 prevailed in group I compared to group II (p = 0.011). The number of newborns with weight from 2000.0 to 2500.0 did not



**Fig. 1.** The condition of the fetus during pregnancy in the study groups.

statistically differ in groups and was 47.6 % (97/204) in group I and 44.0 % (125/284) in group II, respectively ( $p = 0.4373$ ). However, the percentage of children weighing more than 2500 g prevailed in group II, 46.5 % (132/284), compared to 27.5 % (56/204) in group I ( $p < 0.0001$ ). Such features were also reflected in the average percentile of the weight of the newborn, which was also significantly lower in the children of the I group,  $2.8 \pm 0.9$  compared to  $3.7 \pm 1.2$  in the children of group II ( $p < 0.0001$ ).

There was no statistical difference in the gender of newborns between the groups: 45.1 % (92/204) in group I, against 41.9 % (119/284) in group II ( $p = 0.4816$ ).

The number of children with an Apgar score  $<7$  points at 1 minute in group I was greater and amounted to 18.8 % (38/204) in comparison with group II where this indicator was equal to 8.1 % (23/284) ( $p < 0.0001$ ). At 5 minutes, the score on the Apgar scale was  $<7$  points in children in group I in 2.9 % (6/204), and no case in the children in group II.

The need for hospitalization of newborns in the neonatal intensive care unit was 15.7 % (32/204) in group I and 10.2 % (29/284) in group II and had no statistical difference ( $p = 0.1084$ ). The analysis of complications of the early neonatal period showed that their frequency (RDS 10.8 % and 1.8 %; IVH III–IV grade, 2.0 % and 0.0 %; NEC 2.5 % and 0.4 %; sepsis 3.4 % and 0.4 %; the need for inotropic support 3.4 %; and 0.0 %, respectively, in groups I and II) was greater in children of group I compared to group II ( $p < 0.0001$ ). Intranatal death of the fetus was only in 1 case, 0.5 % (1/204) in the group I ( $p = 0.0386$ ). The duration of hospitalization in the intensive care unit was statistically longer in the children of the I group,  $10.7 \pm 2.3$  days, against  $5.2 \pm 1.9$  days in group II ( $p < 0.0001$ ). The total duration of hospitalization in the hospital was also significantly longer in children of the I group compared to group II ( $19.5 \pm 4.8$  days vs.  $9.7 \pm 3.1$  days, respectively) ( $p < 0.0001$ ).

## Discussion

Abnormal fetal growth, the clinical manifestation of FGR, increases the risk of adverse perinatal outcomes, therefore correct prenatal identification of these fetuses is important [14,15,23]. Although there is an agreement among the specialists

of international associations regarding the clinical observation of early and late forms of FGR [1,3], diagnosis of FGR remains an unsolved problem.

Even though in our country, ultrasound examination in the third trimester of pregnancy is a common practice – the result of the conducted study found that before delivery, the diagnosis of FGR was established in 41.8 % of cases, which coincides with the data obtained in France 36.2 % [15], but significantly lower than the results of a recent study in Italy of 75.3 % [16]. Analysis of maternal characteristics did not reveal a significant difference in mean age between the groups, but the mean pregnancy weight and BMI in women of group I was greater compared to group II, in contrast to the data of the European study, where women in the group with FGR identified during pregnancy were more deficient body weight [16]. In the conducted study, both groups were dominated by women giving birth for the first time, but there was no statistical difference between the groups ( $p > 0.05$ ). Extragenital pathology in women of group II was found in only every tenth woman. As for hypertensive disorders, in pregnant women diagnosed with FGR during pregnancy, attention is drawn to a lower frequency of their occurrence (19.6 %), compared to 33.0 % in a European study [16]. These data indicate that the majority of women who were not diagnosed with FGR during pregnancy belong to the low-risk group.

The analysis of the distribution by the period of onset of FGR by group showed a higher percentage of the early form in group I compared to the fetuses of group II ( $p < 0.0001$ ). Similarly, in group I, the proportion of blood flow disorders in the umbilical cord arteries prevailed more than twice (49.5 %) (RI  $> 95$  %), compared to group II ( $p < 0.0001$ ). At the same time, critical blood flow in the arteries of the umbilical cord in group I was detected 3 times more often compared to group II. Such data may indicate more serious damage to the placenta and, as a result, an early manifestation of fetal impairment.

As expected, cesarean section prevailed in women of group I, and in most cases, the indications for operative delivery were precisely signs of fetal distress. Regarding the average birth weight, it was lower in group I compared to group II, which is consistent with the data of European studies [15,16], but the average weight percentile, according to these researchers, was

higher and was 5.0 percentiles, against 2.8 and 3.7 percentiles in the I and II group, respectively. Although the number of children with an Apgar score <7 at 1 and 5 minutes prevailed in children of the I group, the need for hospitalization in the intensive care unit was not significantly different between the groups.

The frequency of early neonatal complications, the length of stay in the intensive care unit, and the total duration of hospitalization were statistically higher in women with antenatally diagnosed FGR ( $p < 0.0001$ ).

## Conclusions

1. The results of the conducted research indicate a low level of prenatal diagnosis of fetal growth restriction (41.8 %). It should be noted that among pregnant women with antenatally undiagnosed fetal growth restriction, a low percentage of somatic pathology (9.2 %) and hypertensive disorders during pregnancy (5.6 %) was established, compared to the group of women with antenatally identified fetal growth restriction (17.2 % and 19.6 %, respectively).

2. Based on the results of childbirth, it was established that among pregnant women with antenatally diagnosed fetal growth restriction, the frequency of its early form was 16.7 %, which was 3.5 times higher than the corresponding indicator in the group with antenatally undiagnosed fetal growth restriction.

3. The most frequent indication for cesarean section operation, regardless of the date of delivery, in both groups were signs of fetal distress, the frequency of which was 1.5 times higher in the antenatally diagnosed fetal growth restriction group.

4. Analysis of the frequency of premature births in the study groups had no statistical difference, however, the increase in the percentage of premature babies in the group with antenatally diagnosed fetal growth restriction (22.5 % compared to 6.0 % in the group with antenatally undiagnosed fetal growth restriction) is due to premature birth due to signs of fetal distress.

5. Perinatal consequences after delivery in the group with antenatally diagnosed fetal growth restriction are characterized by a significantly higher percentage of neonatal complications ( $p < 0.0001$ ), in contrast to the group with antenatally undiagnosed fetal growth restriction, where the gestational age at delivery and birth weight have affected the frequency of early neonatal complications and duration of hospitalization in the neonatal intensive care unit and the hospital.

6. Newborns with undetected growth restriction before delivery have an increased risk of fetal distress, the severity of which is determined by the degree of deterioration of fetal oxygenation, and not by weight percentile, which requires more careful monitoring of fetuses with signs of impaired growth rates in the third trimester of pregnancy.

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