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Newborns in the early neonatal period in a group of mothers at high obstetric and perinatal risk

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ABSTRACT

AIM: We aimed at assessing the status of newborns in the early neonatal period in a group of mothers at high prenatal risk for preeclampsia (PE), fetal growth restriction (FGR), preterm birth (PTB), and fetal chromosomal abnormalities (FCA).

MATERIALS AND METHODS: We prospectively analyzed the status of 435 singletons. Mothers in the first-trimester underwent prenatal screening with risk assessment. Group 1 (study group, *n*=231) included high-risk subgroups for FCA (subgroup 1A, *n*=67), maternal PE (subgroup 1B, *n*=66), FGR (subgroup 1C, *n*=46), and PTB (subgroup 1D, *n*=52). We excluded risk combinations. Group 2 (controls) included 204 children of low-risk women.

RESULTS: Group 1 had a higher incidence of mild-to-moderate asphyxia compared with group 2 (p <0.05) and was more frequent in 1B, 1C, and 1D subgroups. Moreover, the frequency of severe asphyxia was similar between the groups (p >0.05). Intrauterine growth restriction (IUGR) and developmental delay were more frequent in group 1 than in group 2 (p <0.05). Moreover, group 1 children required monitoring and treatment more frequently that in group 2 (p <0.05). The frequency of infectious complications in group 1 and 1A, 1B, and 1C subgroups was equally higher than that of group 2 (p <0.05), while respiratory distress syndrome predominated in group 1 (subgroup 1D) and was not observed in group 2. The discharge rate was 95.7% in group 1 and 84.0% in group 2 (p <0.05). On days 3 to 5, 16% and 3.4% of children in groups 1 and 2, respectively, were transferred to the second stage of aftercare (p <0.05).

CONCLUSIONS: In the early neonatal period, children born to high-risk mothers, as opposed to those born to low-risk mothers, were significantly more likely to have asphyxia, IUGR, infectious complications, and indications for continued treatment in the second stage of nursing.

Keywords: asphyxia; intrauterine growth; intrauterine growth restriction; newborns; prenatal screening; risk level.

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Новорождённые в раннем неонатальном периоде в группе матерей высокого акушерского и перинатального риска

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АННОТАЦИЯ

Цель исследования — оценить состояние новорождённых в раннем неонатальном периоде в группе матерей высокого пренатального риска по развитию преэклампсии (ПЭ), задержки роста плода (ЗРП), преждевременных родов (ПР) и хромосомных аномалий у плода (ХА).

Материалы и методы. Проведён проспективный анализ состояния новорождённых от 435 одноплодных родов. Матерям в I триместре выполнен пренатальный скрининг с оценкой риска. В 1-ю, основную группу (n=231) включили подгруппы с высоким риском по развитию ХА у плода — подгруппа 1A (n=67), ПЭ у матерей — подгруппа 1B (n=66), ЗРП — подгруппа 1C (n=46), ПР — подгруппа 1D (n=52). Исключены сочетания рисков. Вторая, контрольная группа включала 204 ребёнка от женщин с низким риском.

Результаты. В 1-й группе отмечена более высокая частота рождения детей в состоянии асфиксии лёгкой и средней степени, чем во 2-й группе (p <0,05), и чаще в подгруппах 1B, 1C и 1D. Частота тяжёлой асфиксии не имела отличий между группами (p >0,05). Задержка внутриутробного роста и развития (ЗВУР) в 1-й группе встречалась чаще, чем во 2-й (p <0,05). Наблюдение и лечение потребовалось детям 1-й группы чаще, чем детям 2-й группы (p <0,05). Частота инфекционных осложнений у детей в 1-й группе и в подгруппах 1A, 1B и 1C оказалась выше, чем во 2-й группе (p <0,05). Респираторный дистресс-синдром преобладал в 1-й группе в подгруппе 1D, во 2-й группе он не отмечен. Выписаны 84,0% детей 1-й группы и 95,7% детей 2-й группы (p <0,05). На 3–5-е сутки 16% детей 1-й группы переведены на 2-й этап долечивания, во 2-й группе — 3,4% (p <0,05).

Заключение. У детей, рождённых от матерей с высоким риском, в отличие от рождённых от матерей с низким риском, в раннем неонатальном периоде достоверно чаще отмечены асфиксия, ЗВУР, инфекционные осложнения и показания к продолжению лечения на втором этапе выхаживания.

Ключевые слова: асфиксия; внутриутробное развитие; задержка внутриутробного роста; новорождённые; пренатальный скрининг; степень риска.

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ЭКО•ВЕКТОР

BACKGROUND

Prediction based on the results of prenatal screening of adverse complications for both pregnant women and the fetus is one of the most pressing and difficult tasks in the perinatal period [1]. Nowadays, combined screening is used for this purpose, consisting of calculating the basic risk based on the patient's age with subsequent correction of its data considering biochemical markers and ultrasound results [2]. Protein and hormone levels in the fetoplacental system are measured to assess the condition of the fetus from the early stages and throughout pregnancy [3–5]. Prenatal screening in trimester I includes determining placental hormones that indicate its function, namely, free β-subunit of human chorionic gonadotropin (β-hCG), glycoprotein pregnancy-associated plasma protein-A (PAPP-A) [6], and nuchal fold thickness (NFT) [7]. An increasing number of studies have focused on determining the prognostic significance of prenatal screening and expanding diagnostic capabilities for the fetus [8–10]. Fetal losses and the development of intrauterine growth restriction (IUGR) during pregnancy increase with a decrease in free β-hCG and PAPP-A levels and an increase in NFT [11–14]. IUGR is a serious problem in obstetrics, neonatology, and pediatrics [15]. This complication in the perinatal period becomes a significant risk factor for death in the neonatal and postneonatal periods, the incidence of which increases sharply and is 3–10 times higher than the mortality rate of newborns with normal development [16–19]. The diagnostic criterion for IUGR is considered to be a decrease in body weight (as an integral indicator of fetal size) and/or body length less than the 10th percentile compared to that for gestational age [20]. Research shows that IUGR diagnosed in the fetus has long-term negative effects on the endocrine system, neurological development, and homeostasis in the newborn [21]. Growth disturbances, low weight, decreased head circumference, and visual impairment are more often recorded in infants with IUGR than in those with normal development at aged 18–22 months [22]. Furthermore, a predisposition in adult life to obesity, hypertension, cardiovascular diseases, and diabetes mellitus has been noted [23].

Studies examining the significance of high-risk mothers based on prenatal screening in trimester I in predicting the characteristics of the condition of newborns are advisable.

This study aimed to evaluate the condition of newborns in the early neonatal period in a group of mothers at high prenatal risk for preeclampsia, fetal growth restriction, preterm birth, and chromosomal abnormalities in the fetus.

MATERIALS AND METHODS

A prospective analysis of the condition of newborns from 435 births in singleton pregnancies was performed. All patients in the trimester I of pregnancy (11 weeks and 4 days to 13 weeks and 6 days) underwent prenatal screening. Depending on the level of identified risk, the patients (*n*=435) were divided into two groups: the main group (risk frequency of 1:100 and above [high risk]) and control group (risk frequency of 1:101 and below [low risk]). The study was conducted at V.V. Veresaev City Clinical Hospital (clinical base of the Department of Obstetrics and Gynecology No. 1 of the I.M. Sechenov First Moscow State Medical University), which provides second (expert) level of prenatal diagnostics.

The main group included 231 newborns from patients (*n*=231) in whom screening revealed a high risk of preeclampsia (PE), fetal growth restriction (FGR), preterm birth (PTB), and fetal chromosomal abnormalities (FCA). The control group included 204 newborns from patients (*n*=204) with a low risk of prenatal screening for the development of complications. The pregnant women with a high risk of only one of the four assessed outcomes were selected, and subgroups were formed. In the main group, four subgroups were formed: 1A (*n*=67), newborns from pregnant women with a high risk of FCA; 1B (*n*=66), newborns from pregnant women with a high risk of PE; 1C (*n*=46), newborns from pregnant women with a high risk of FGR; and 1D (*n*=52), newborns from pregnant women with a high risk of PTB. Combined screening included assessment of blood flow in the uterine arteries, the condition of the internal orifice of the uterus, and the presence or absence of uterine hypertonicity. In the fetus, the length of the nasal bone, coccygeal–parietal size (CPS), NFT, and heart rate were assessed. Ultrasound (US) examination was performed in the Department of Antenatal Fetal Care of the branch of the V.V. Veresaev City Clinical Hospital using ALOKA PROSOUND α 6 (Hitachi Aloka Medical, Ltd., Japan), APLIO 500 (Toshiba Medical Systems Corporation, Japan), and GE Voluson E6 (GE Healthcare, USA). In parallel, β-hCG, pregnancy-associated plasma protein-A (PAPP-A), and human placental growth factor concentrations were determined in the blood serum of pregnant women. Prenatal screening was performed according to the order of the Ministry of Health of Russia no. 1130n, dated October 20, 2020, and the order "On improving the organization of prenatal (antenatal) diagnostics of fetal/child development disorders", dated June 14, 2013, no. 600 [24]. A unified network of the Astraia software and hardware complex was used to evaluate the results of prenatal screening.

The criteria for including pregnant women in the groups were high and low risk of prenatal screening for FCA in the fetus, development of PE, FGR, and PTB based on test results in trimester I, birth of a child without FCA, singleton pregnancy, spontaneous pregnancy, and absence of severe concomitant extragenital diseases. The exclusion criteria were chromosomal abnormalities confirmed antenatally and/or after the birth of the child, multifetal pregnancy, and pregnancy resulting from ART.

A clinical assessment of the condition of newborns was performed in the early neonatal period and during the first 3 days of life. After birth, the main integral indicators were determined, namely, Apgar scores at minutes 1 and 5 of life to describe the cardiorespiratory and neurological condition

of the newborn, degree of asphyxia [25], weight and height at birth, weight loss on day 3 of life, and incidence and structure of neonatal morbidity. To assess the compliance of the child's anthropometric indicators with the appropriate values, percentile graphs and tables of I.E. Olsen (2010), T.R. Fenton (2013), and Intergrowth-21st. (2014) [26] were used, and gender differences were considered [27]. To assess IUGR severity, we used the classification according to the National Guidelines for Neonatology [15]. Degree 1 of severity (mild) was characterized by a decrease in body weight below the 10th percentile with normal or moderately reduced body length. In degree 2 of severity (moderate), both body weight and length decreased, with the indicators being in the range from the 10th to the 3rd percentile. Degree 3 (severe) was characterized by a decrease in all parameters of physical development below the third percentile.

All female patients in the study groups underwent clinical and laboratory examinations, as regulated by the order of the Ministry of Health of Russia no. 1130n.

All patients included in the study signed a voluntary informed consent form to participate in the study and publish their medical data. This study was approved by the local ethics committee of I.M. Sechenov First Moscow State Medical University (LEC protocol dated January 22, 2021, no. 01-21).

Statistical analysis of data was performed using the computer program STATISTICA 64 bit for Windows and the statistical functions of Microsoft Office Excel 2007. The analysis of the results was presented in the form of arithmetic means and root-mean-square deviations. When comparing the average values of two groups of unrelated samples, subject to the law of normal distribution, Student's *t*-test was used. Differences in frequencies were considered statistically significant at $p < 0.05$.

RESULTS

The average age of patients was 29.1 ± 2.1 years in the main group and 30.2 ± 1.1 years in the control group; the groups did not have statistically significant differences in age ($p > 0.05$). Moreover, primigravidas in the high-risk subgroups and control group did not have statistically significant differences (30% versus 33%) ($p > 0.05$).

In addition, 433 (99.54%) of the 435 women examined had liveborn infants; 2 (0.46%) patients in the main group had stillbirths. In the group with high prenatal risk, the incidence of antenatal fetal death (AFD) was significantly different ($p < 0.05$). No cases of fetal losses were found in the subgroups with a high risk of developing PE (1B) or PTB (1D). AFD at weeks 29 and 30 was associated with progressive chronic placental insufficiency (PI), which was confirmed by histological examination of the placentas (placental hypoplasia, many afunctional zones, infarction, and ischemia).

Basic medical care for newborns was provided in the delivery room. The birth of children with varying degrees of asphyxia was noted in the high-risk group in 44 (19.0%) cases and in the control group in 15 (7.4%) cases. The indicators showed statistically significant differences ($p < 0.05$). The incidence of mild asphyxia in subgroups 1C (12.8%) and ID (21.2%) was significantly higher than that in the control group (3.9%; $p < 0.05$). The birth of children with moderate asphyxia prevailed in subgroups 1B (7.6%), 1C (8.5%), and 1D (15.4%) and was significantly different ($p < 0.05$) compared to that in the control group (2.5%). The frequency of birth of children with severe asphyxia did not differ significantly and was 1.3% in the main group and 1% in the control group ($p > 0.05$).

Thus, the birth of children with asphyxia of varying severity was more often observed in the group of women with high perinatal risk, especially in subgroups with high risk for PE, FGR, and PTB. The data is presented in Table 1.

Considering the requirements of modern clinical recommendations, acetylsalicylic acid (aspirin) was prescribed to pregnant women with a high risk of perinatal complications for prophylactic purposes, which improves the depth of placentation and blood flow in the spiral arteries of the uterus [28–29]. All pregnant women with identified risk factors in group 1 (subgroups) and group 2 were prescribed low doses of aspirin, that is, 150 mg/day from week 14 to 36,

Table 1. Indicators of the condition of newborns (the number of newborns by groups. with an assessment of the condition on the Apgar scale in points. M±σ)

Indicator	Group 1 (*n*=231). *n* (%)					Group 2 (*n*=204), *n* (%)
	1A. FCA (*n*=67)	1B. PE (*n*=66)	1C. FGR (*n*=46)	1D. PB (*n*=52)	Group 1	
Satisfactory condition	63 (92.6±1.8)	58 (87.9±2.1)	35 (74.5±2.9)	31 (59.6±3.2)*	187 (80.2±2.6)	189 (92.6±2.0)*
Mild asphyxia	3 (4.4±1.3)	3 (4.6±1.4)	6 (12.8±2.9)*	11 (21.2±2.7)*	23 (9.9±1.9)*	8 (3.9±1.3)*
Moderate asphyxia	1 (1.5±0.8)	5 (7.6±1.7)*	4 (8.5±1.8)*	8 (15.4±2.4)*	18 (7.8±1.7)*	5 (2.5±1.1)*
Severe asphyxia	0	0	1 (2.1±0.9)	2 (3.9±1.3)	3 (1.3±0.7)	2 (1.0±0.7)
Stillbirth	1 (1.5±1.1)	0	1 (2.1±1.3)*	0	2 (0.9±0.8)	0

*Differences between Group 1, Group 1 subgroups, and Group 2 are significant ($p < 0.05$); FCA, fetal chromosomal abnormalities; PE, preeclampsia; FGR, fetal growth retardation; PB, preterm birth.

considering compliance with the instructions for use of the drug in the Russian Federation.

Anthropometric assessment showed that the frequency of births of children with IUGR in the main group was 84 (33.0%) cases compared to 34 (18.3%) cases in the control group; the differences were statistically significant (p <0.05). In the IUGR group, morphological signs of PI, which became the probable cause of FGR, were found in 64 (76.2%) patients (Table 2).

The birth of large children weighing >4,000 g was significantly more often noted in the control group than in the main group, with 47 (22.6%) cases and 7 (3.0%) cases, respectively (p <0.05).

Among all the examined children, 19.1% of newborns from mothers in the high prenatal risk group and 7.3% from the control group required follow-up and medical care in the early neonatal period; these indicators showed significant differences (p <0.05). The frequency of treatment for newborns in the neonatal intensive care unit (NICU) and the unit for neonates and prematurely born children (UNP) was higher in children from mothers in the group with high prenatal risk (9.1% and 10.0%, respectively) than in those from mothers in the control group (3.4% and 3.9%); the indicators had significant differences (p <0.05). The routing of newborns on day 1 of life is presented in Table 3.

When analyzing the course of the early neonatal period, the incidence of complications was significantly higher in children from high-risk mothers and amounted to 20.8% versus the control group value of 3.4% (p <0.05). In the structure of complications, the share of infectious complications in the main group (7.8%) and subgroups 1A, 1B, and 1C was 6.0%, 7.6%, and 17.4%, respectively, and was significantly higher than that in the control group (1.0%; p <0.05). The incidence of neonatal aspiration of amniotic fluid did not have significant differences between the groups, and it was not noted in subgroups with a high risk of FGR and PTB (p > 0.05). In subgroups 1C and ID, the incidence of complications, such as hemorrhagic syndrome, was 2.2% and 5.8%, and that of respiratory distress syndrome (RDS) was 4.4% and 38.5%, respectively, and was higher compared to that of subgroup 1A and the control group and had statistically significant differences (p <0.05). Complications such as hemorrhagic syndrome and RDS were not determined in the control group. Table 4 shows the structure of the complications.

Newborns from mothers from the high prenatal risk group were discharged from the maternity hospital in satisfactory condition in 194 (84.0%) cases; in the control group, newborns in 197 (96.6%) of cases were discharged, and the indicators revealed statistically significant differences (p <0.05). In the main group, 37 (16.0%) newborns on days 3–5 of life required transfer for continued treatment and follow-up to the NICU of the stage 2 nursing or to the stage 2 nursing newborns; whereas in the control group, there were 7 (3.4%) such cases, with significant statistical differences between the indicators (p <0.05). The data are presented in Table 5.

At stage 2, 21 newborns of the main group and 1 newborn of the control group were treated in the NICU; the indicators had significant differences (p <0.05). Follow-up and treatment in stage 2 nursing newborns was required in 16 children of the main group and 6 children of the control group; the differences were significant (p <0.05).

Table 2. Number of newborns with intrauterine development delay, M±σ

Показатель	Group 1 (n=231). n (%)					Group 2 (n=204), n (%)
	1A. FCA (n=67)	1B. PE (n=66)	1C. FGR (n=46)	1D. PB (n=52)	Group 1	
Degree 1 IUGR	20 (29.4±2.6)	9 (13.6±2.2)	11 (23.4±2.7)*	12 (23.1±2.8)*	52 (22.1±2.7)*	28 (13.5±2.4)*
Degree 2 IUGR	8 (10.3±2.0)*	4 (6.1±1.6)	5 (8.5±1.8)*	5 (9.6±1.9)*	22 (8.6±1.8)	6 (4.8±1.5)*
Degree 3 IUGR	6 (8.7±1.8)	1 (1.5±0.8)	1 (2.1±0.9)	2 (3.9±1.3)	10 (2.3±1.0)	0

*Differences between Group 1 and Group 2 subgroup values are significant (p < 0.05); FCA, fetal chromosomal abnormalities; PE, preeclampsia; FGR, fetal growth restriction; PB, preterm birth; IUGR, intrauterine growth restriction.

Table 3. Routing of newborns by departments in the early neonatal period, M±σ

Characteristics	Group 1 (n=231). n (%)					Group 2 (n=204), n (%)
	1A. FCA (n=67)	1B. PE (n=66)	1C. FGR (n=46)	1D. PB (n=52)	Group 1	
Rooming-in	63 (94.0±1.6)	58 (87.9±2.2)	35 (77.1±2.8)*	31 (59.6±3.2)*	187 (81.0±2.3)*	189 (92.7±1.8)*
Follow-up and treatment of UNP	3 (4.5±1.4)	3 (4.6±1.4)	6 (13.0±2.2)*	11 (21.2±2.7)*	23 (10.0±2.0)*	8 (3.9±1.3)*
Follow-up and treatment in the NICU	1 (1.5±0.8)	5 (7.6±1.7)	5 (10.9±2.1)*	10 (19.2±2.6)*	21 (9.1±1.9)	7 (3.4±1.3)*

*Differences between Group 1 and Group 2 subgroup values are significant (p < 0.05); FCA, fetal chromosomal abnormalities; PE, preeclampsia; FGR, fetal growth restriction; PB, preterm birth; UNP, unit for neonatal and premature children; NICU, neonatal intensive care unit.

Table 4. Number of newborns with complications of the early neonatal period, M±σ

Complication	Group 1 (*n*=231), *n* (%)					Group 2 (*n*=204), *n* (%)
	1A, FCA (*n*=67)	1B, PE (*n*=66)	1C, FGR (*n*=46)	1D, PB (*n*=52)	Group 1	
Intrauterine infection of an unspecified etiology	3 (4.5±1.4)*	1 (1.5±0.8)	3 (6.5±1.6)*	0	7 (3.0±1.1)*	1 (0.5±0.5)*
Intrauterine pneumonia	1 (1.5±0.8)	4 (6.1±1.6)*	5 (10.9±3.0)*	1 (1.9±0.9)	11 (4.8±1.4)*	1 (0.5±0.5)*
Neonatal aspiration	1 (1.5±0.8)	3 (4.6±1.4)	0	0	4 (1.7±0.9)	5 (2.5±1.1)*
Hemorrhagic syndrome	0	2 (3.0±1.1)*	1 (2.2±1.0)*	3 (5.8±1.5)*	6 (2.6±1.1)*	0*
Respiratory distress syndrome	0	0	2 (4.4±1.3)	20 (38.5±3.2)*	22 (9.5±1.9)	0*

*Differences between Group 1 subgroup and Group 2 values are significant (p <0.05); FCA, fetal chromosomal abnormalities; PE, preeclampsia; FGR, fetal growth retardation; PB, preterm birth.

Table 5. Transfer of newborns to the second stage of further treatment — number of children. abs. (%)

Characteristics	Group 1 (*n*=231), *n* (%)					Group 2 (*n*=204), *n* (%)
	1A, FCA (*n*=67)	1B, PE (*n*=66)	1C, FGR (*n*=46)	1D, PB (*n*=52)	Group 1	
Discharged home	64 (95.5±1.4)	60 (90.9±1.9)	37 (80.4±2.6)	33 (63.5±3.1)	194 (84.0±2.4)*	197 (96.6±1.3)*
Transfer to the NICU of stage 2 nursing	1 (1.5±0.8)	5 (7.6±1.7)	5 (10.9±2.0)*	10 (19.2±2.6)*	21 (9.1±1.9)*	1 (0.5±0.5)*
Transition to stage 2 of nursing newborns	2 (3.0±1.1)	1 (1.5±0.8)	4 (8.7±1.8)*	9 (17.3±2.5)*	16 (6.9±1.7)*	6 (2.9±1.2)*

**Differences between Group 1 subgroup and Group 2 values are significant (p <0.05); FCA, fetal chromosomal abnormalities; PE, preeclampsia; FGR, fetal growth restriction; PB, preterm birth; UNP, unit for neonatal and premature children; NICU, neonatal intensive care unit.

Studying the prognostic aspects of prenatal screening to increase the efficiency of prenatal monitoring and the earliest possible diagnostics of pregnancy complications will allow early diagnosis of adverse consequences for the fetus, which may subsequently affect the condition of newborns.

CONCLUSION

In the group of mothers with high prenatal risk, more children were born with asphyxia, especially in subgroups with a high risk for the development of PE, FGR, and PTB and children with IUGR in subgroups with a high risk for FCA, PE, FGR, and PTB compared with the control group (p <0.05). Complicated course of the early neonatal period in newborns was significantly more common in the group with a high risk of prenatal screening than in the control group (p <0.05). Newborns from mothers at a high perinatal risk for the development of PE, FGR, PTB, and FCA in the fetus more often required follow-up and treatment in the early neonatal period than the group of children from mothers with a low risk, which indicates a decrease in the adaptive capabilities of these children.

ADDITIONAL INFORMATION

Authors' contribution. All the authors made a substantial contribution to the conception of the work, acquisition, analysis, interpretation of data for the work, drafting and revising the work, final approval of the version to be published and agree to be accountable for all aspects of the work.

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ДОПОЛНИТЕЛЬНО

Вклад авторов. Все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед публикацией.

Финансирование. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

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