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On the issue of risk stratification of early and late forms of fetal growth restriction

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Abstract

Summary: It should be noted that fetal growth restriction syndrome plays a significant role in the formation of the structure of perinatal morbidity and mortality, the frequency of which, according to domestic authors, ranges from 5 to 17 %, among full-term infants – from 5% to 22 %, among preterm infants – from 18 to 24 %. About 30 million children are born with this diagnosis annually in the world.

Aim: To establish the prevalence, frequency and proportion of prognostically significant predisposition factors for the development of early and late fetal growth restriction; to identify the most significant of them for the prediction of this syndrome.

Materials: Two comparable groups were formed: group 1 – 159 cases (26.7 %) of early fetal growth restriction (up to 32 weeks of gestation) and group 2 – 437 cases (73.3 %) of late fetal growth restriction. The control group included 80 patients who gave birth to a full-term baby with average weight parameters in the population. The work was performed in the format of a longitudinal retrospective case-control study. The statistical analysis of the data was performed using Microsoft Office XP application packages for statistical processing of the material – Microsoft Excel (version 7.0), and the odds ratio (OR) for the occurrence of comparable values or signs was also given.

Results: 654 documented forms of birth of children with FGR (2.8 %) were retrospectively analyzed, an increase in FGR cases by 1.8 times was noted. The most significant risk factors for the development of fetal growth restriction were identified, including heredity and FGR in previous pregnancy (OR – 3.11), socioeconomic factors and psycho-emotional cofounders (OR – 2.76), harmful tobacco smoking (OR – 2.47), age over 35 years (OR – 2.82), multiple pregnancy (OR – 7.83), underweight (OR – 3.69), cardiovascular disease (OR – 16.32), anaemia (OR – 2.32), placental dysfunction (OR – 3.12), umbilical cord pathology and peculiarities of its insertion (OR – 3.77). The following factors characterising a woman's reproductive health and factors related to the course of pregnancy were associated with the risk of early

FGR: sexual infantilism (OR – 2.46), uterine factor and infertility (OR – 2.19), first pregnancy in age over 35 years (OR – 2.28), spontaneous abortion and habitual miscarriage (OR – 2.11), instrumental intrauterine interventions (OR – 2.74), and previous pregnancy with FGR (OR – 3.04). An important predictor of FGR after 32 weeks of gestation (OR – 3.01) was social factors (bad habits, high levels of chronic stress and psychotraumatic factors related to martial law, internal and external migration, and family financial situation). Fetal and placental factors, including: placental dysfunction (OR – 2.0), intrauterine infection (OR – 1.62), umbilical cord pathology and features of its insertion (OR – 3.04), fetal malformations (OR – 2.20) formed risk groups for both early and late forms of FGR.

Conclusions: It is undeniable that the range of factors leading to the development of fetal growth restriction is quite wide and multifaceted. Factors associated with reproductive health disorders and complicated pregnancy are important for the development of early FGR, while fetal and placental factors are equally predictive of both early and late forms of this syndrome.

Keywords: Fetal growth restriction, risk factors, placental dysfunction, umbilical cord pathology, pregnancy complications, reproductive health.

Introduction

It should be noted that fetal growth restriction syndrome plays a significant role in the formation of the structure of perinatal morbidity and mortality, the frequency of which, according to domestic authors, ranges from 5 to 17 % [1-3], among full-term infants – from 5 to 22 %, among preterm infants – from 18 to 24 %, and about 30 million children are born with this diagnosis annually worldwide [4-6]. This clinical condition dominates mainly in Central Asia, where it is about 31 %, 20% in Africa, 5 % in Latin America, and up to 6.5-7 % in developed European countries [1, 2, 4, 7]. The incidence of FGR in the population is variable, with some authors reporting 3-5 % of cases in practically healthy pregnant women; with a complicated pregnancy or a burdened history progressively increasing to 10-25 %, causing every third case of antenatal death and leading to an increase in perinatal mortality by more than 8 times [4, 6, 7, 8].

It should be noted that FGR carries a rather high perinatal burden, accompanying disorders of psychomotor development of such children in the future (behavioural disorders, emotional-volitional and motor disorders, cognitive and attention disorders, aggression, asthenic syndrome) [4, 9, 10]. Long-term consequences include neuropsychiatric developmental disorders, deviations in weight and height, cardiovascular diseases, and metabolic conditions in adulthood [4, 9, 10].

According to the term of formation, early and late forms of FGR are distinguished, which demonstrate different pathogenetic moments of development – from incomplete invasion of the trophoblast into the myometrial segment of the spiral arteries, the absence of their physiological gestational changes, spasm and alteration of the vascular wall with impaired blood circulation in the interventricular space, microcirculation and ischaemia in the early form of FGR – to disruption of the uteroplacental-fetal circulation component with the development of chronic hypoxia and redistribution of fetal blood flow with predominance of fetal brain perfusion in the late form of FGR [8, 11, 12, 13, 14].

Early FGR accounts for 20-30% of all cases, and in

50% of cases, this form is combined with preeclampsia and placental dysfunction [4, 15]. In contrast, late FGR accounts for 70-80% of all cases of this complication of pregnancy, which has a more favourable course, is accompanied by moderate placental dysfunction with minor abnormalities in umbilical artery Doppler, but unpredictable sudden deterioration in the fetal condition in the last weeks of gestation or during labour [4, 13, 16].

The identification of reliable prognostic criteria for perinatal outcomes, as well as methods of medical correction with proven efficacy, remain controversial and require further research [17]. High perinatal morbidity and mortality among full-term and premature newborns with FGR indicates the imperfection of existing diagnostic methods, the lack of evidence-based medical approaches, and criteria for optimal delivery time, which determines the relevance of this study. Given the current lack of effective methods of treating this pathological condition, prognosis and timely prevention remain the leading areas of obstetric support of pregnancy with fetal growth restriction and the only means of reducing perinatal mortality and a component of a rehabilitation program in the future.

The aim of the study

To determine the prevalence, frequency and proportion of prognostically significant predisposition factors for the development of early and late fetal growth restriction, to identify the most significant of them for the prediction of this syndrome.

Materials and methods

This work was carried out in the period from 2020 to 2024 at the Kyiv Perinatal Centre; the study material included medical records of 23171 birth histories, partograms and newborn histories, where 654 documentary forms of birth of children with fetal growth restriction (2.8%) were retrospectively analysed (Figure 1).

There was a 1.8-fold increase in the number of

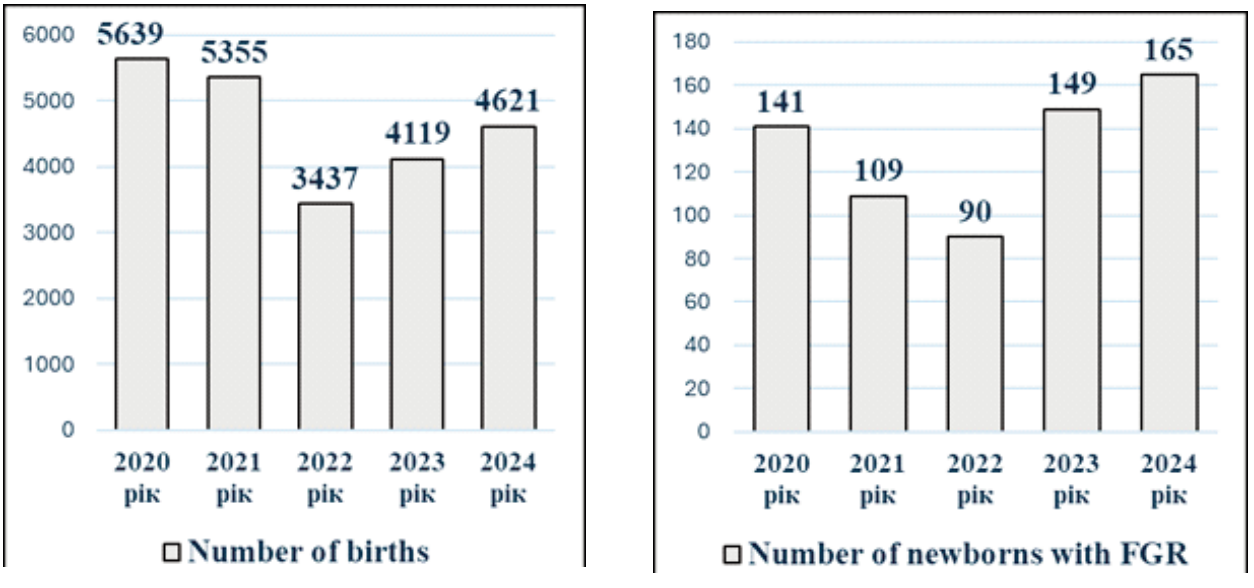

Figure 1. Number of births and newborns with fetal growth restriction in 2020-2024, abs. n.

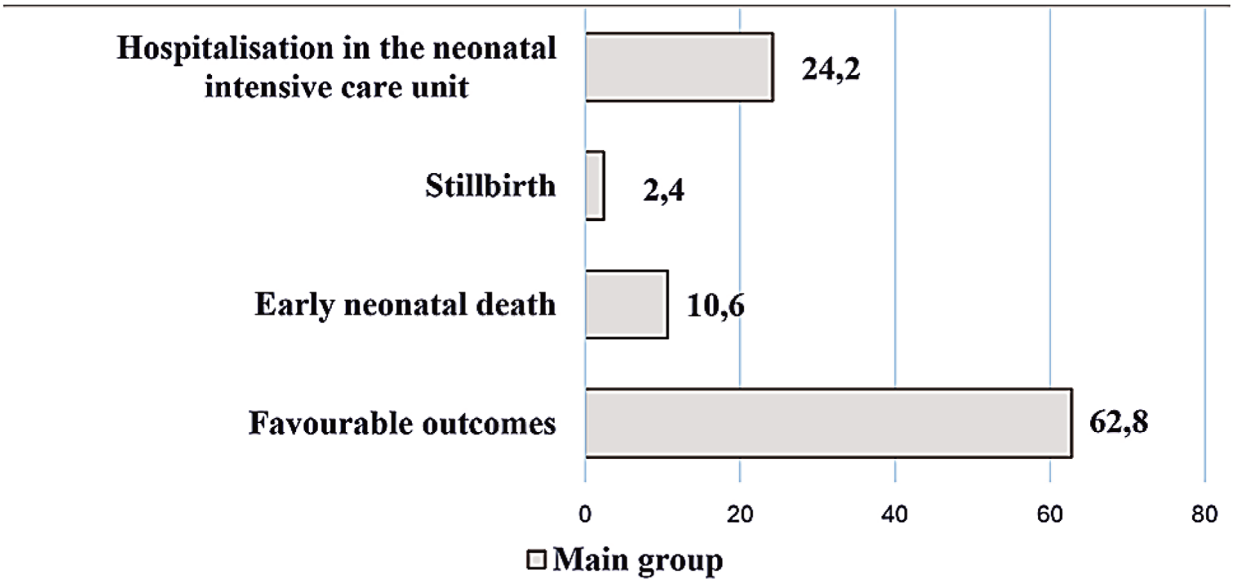

Figure 2. Structure of perinatal outcomes in the main group, n=654, %.

cases of FGR; 158 babies (24.2%) were hospitalised in the neonatal intensive care unit; stillbirth was in 16 cases (2.4%); early neonatal death – in 69 cases (10.6%); and favourable outcomes – in 411 cases (62.8%) (Figure 2).

Two comparable groups were formed: group 1 – 159 cases (26.7 %) of early fetal growth restriction (up to 32 weeks of gestation) and group 2 – 437 (73.3 %) cases of late fetal growth restriction. The control group included 80 patients who gave birth to

Table 1. Stratification of risk factors for early and late fetal growth restriction, abs. n., %, n= 596

Indicators	**Group 1 (n=159)**	**Group 2 (n=437)**	**χ^2, p**
Age, years	33.6 ± 2.4	26.7 ± 1.6	p1>0.05, p<0.05
First-time mothers over the age of 30	82 (51.6 %)	139 (31.8 %)	χ2=18.68, p<0.001
Heredity	94 (59.1 %)	278 (63.6 %)	χ2=0.82, p>0.3
Infertility and IVF programs	59 (37.1 %)	89 (20.4 %)	χ2=16.62, p<0.001
Habitual miscarriage	26 (16.4 %)	37 (8.5 %)	χ2=6.88, p<0.01
BMI > 20.0 kg/m2	59 (37.1 %)	97 (22.5 %)	χ2=12.65, p<0.001
Gestational weight gain < 7 kg	46 (28.9 %)	77 (17.6 %)	χ2=8.43, p<0.005
Fetal malformations	18 (11.3 %)	24 (5.5 %)	χ2=5.19, p<0.02
Retroplacental haematomas	46 (28.9 %)	74 (16.9 %)	χ2=9.70, p<0.002
Pathology of the umbilical cord and its insertion	45 (28.3 %)	108 (24.7 %)	χ2=0.61, p>0.4
Sexual infantilism	49 (30.8 %)	67 (15.3 %)	χ2=16.86, p<0.001
Uterine factor	68 (42.8 %)	111 (25.4 %)	χ2=15.92, p<0.001
Intrauterine infection	52 (32.7 %)	101 (23.1 %)	χ2=5.13, p<0.02
Arterial hypertension and preeclampsia	57 (35.8 %)	69 (15.8 %)	χ2=26.95, p<0.001
Metabolic syndrome	39 (24.5 %)	34 (7.8 %)	χ2=28.89, p<0.001
Acute respiratory viral infection	59 (37.1 %)	71 (16.2 %)	χ2=28.53, p<0.001

a full-term baby with a weight corresponding to the average population parameters for a gestational age of 38-41 weeks.

Inclusion criteria for the study: patients over 18 years of age diagnosed with fetal growth restriction, where this syndrome is verified on the basis of the results of clinical, instrumental, functional and laboratory methods of research based on a slowdown in the growth of the predicted fetal weight (PFW), more than two standard deviations in the dynamics and/or abdominal circumference (AC) < 10th percentile in combination with impaired blood flow or PFW and/or AC < 3rd percentile); gestational age over 22 weeks, consent to participate in the study. Exclusion criteria – autoimmune diseases, severe extragenital and oncological diseases, diabetes mellitus, active infectious process, refusal to participate in the study.

The most complete and accurate diagnostic criteria for early and late FGR are the factors proposed by the International Society of Ultrasound in Obstetrics and Gynecology and approved by national clinical guidelines [13, 18-20]. According to expert consensus, early and late FGR is determined using the Delphi procedure [20]. Three separate parameters (abdominal circumference (AC) < 3rd centile, estimated fetal weight (EFW) < 3rd centile, and absence of end-diastolic blood flow in the umbilical artery (UA)) and four additional parameters (AC or EFW < 10th centile in combination with a pulsatility index (PI) > 95th centile in either the UA or uterine artery) were agreed upon for early FGR (< 32 weeks). The forms differ in clinical presentation, ultrasound and pathological features [20].

For the diagnosis of early FGR, it is sufficient to detect one of the factors before 32 weeks of pregnancy: PFW and/or AC < 3rd percentile, or zero umbilical cord artery systolic-diastolic blood flow, or a combination of PFW and/or AC < 10th percentile with a pulsatility index in the uterine artery and/or umbilical artery greater than 95th percentile [20]. Late FGR is diagnosed at 32 weeks or later by one absolute criterion (PFW and/or AC < 3rd percentile) or by two of the three relative criteria (PFW and/or AC

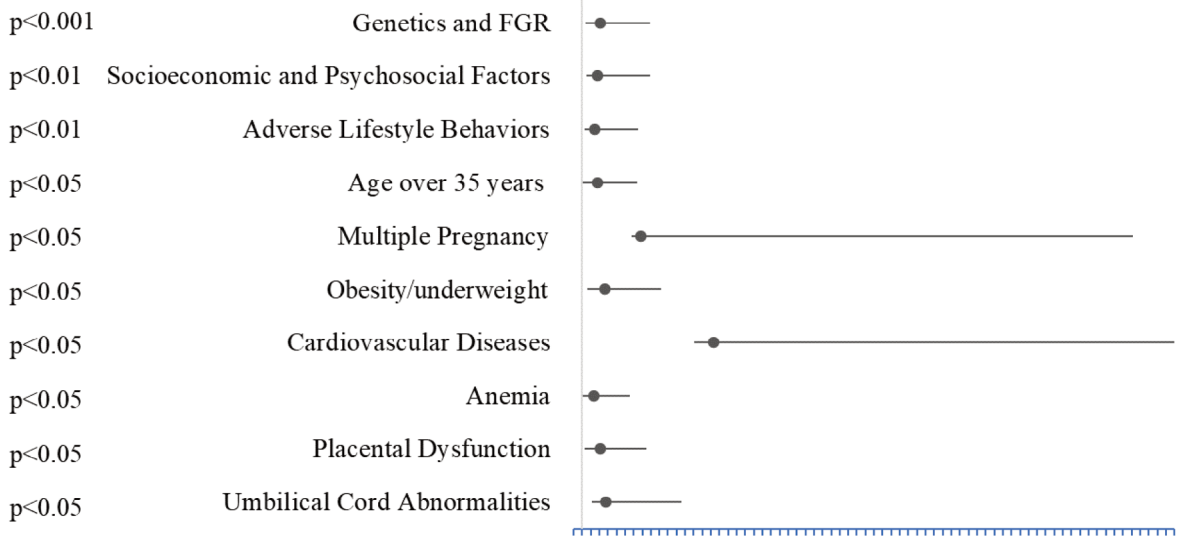

Figure 3. Forest plot of the odds ratio of the risk of fetal growth restriction.

< 10th percentile, slower growth rate of PFW and/or AC that crosses more than two quartiles on percentile growth charts); cerebral-placental ratio < 5th percentile or pulsatility index in the umbilical artery greater than 95th percentile [13, 18, 19, 21].

The information obtained on clinical and social characteristics, somatic and gynecological diseases, menstrual function and its formation, parity of births, reproductive and obstetric history, the course of this pregnancy, gestational complications, fetometry and Doppler data, the course of labour and the method of delivery, obstetric and perinatal outcomes were evaluated.

The work was carried out in the format of a longitudinal retrospective case-control study. The statistical analysis of the data was performed using Microsoft Office XP application packages for statistical processing of material – Microsoft Excel (version 7.0) and Statistica statistical processing software (version 6.0), taking into account computational methods recommended for biology and medicine. The paper also presents the odds ratio (OR) of occurrence of the compared values or traits, where the single-factor binary logistic regression model was used to construct 95% confidence intervals (95% CI) and point estimates of OR, OR was considered statistically significant if the 95% CI did not include one.

Results

A retrospective analysis of 23,171 births that took place at the Kyiv Perinatal Centre in 2020-2024 was performed. Fetal growth restriction was diagnosed in 654 cases (2.8 %) of pregnant women, including 58 cases with multiple pregnancies (OR – 7.83; 0.95 % CI: 1.07-57.33, p<0.05).

Pregnancy with the birth of a fetus with FGR was more common in women aged 18 to 20 years and in age over 35 years (403-61.6 %) (OR – 2.82; 0.95 % CI: 1.74-4.57, p<0.05). Tobacco smoking increased the risk of FGR by 2.5 times (OR – 2.47; 0.95 % CI: 1.21-5.06, p<0.02).

The investigation of the clinical and social characteristics of the study group of patients demonstrated

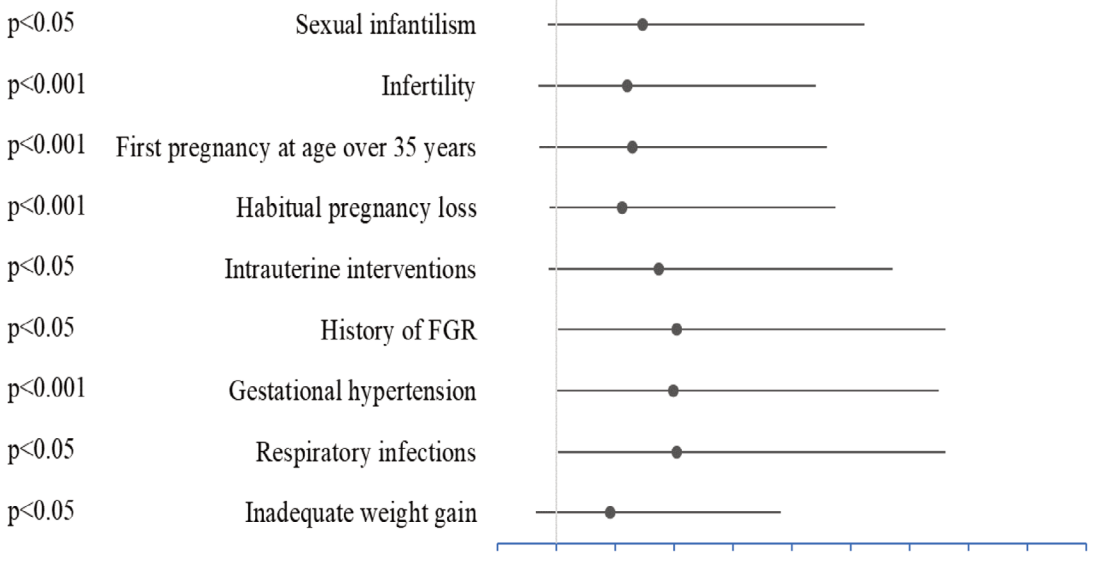

Figure 4. Forest plot of the odds ratio of the risk of early fetal growth restriction by factors characterizing reproductive health and related to the course of pregnancy.

the importance of social factors: features of social status (living in rural areas, low level of education, housewives and unemployed in the professional sphere), which are important in the degree of women's awareness of reproductive health issues; a high percentage of women from the internal migration group, which allowed us to identify these characteristics as significant psycho-emotional cofounders (OR – 2.76; 0.95 % CI: 1.24-6.14, p<0.01).

Fetal growth restriction is a structural component of placenta-associated pregnancy complications and part of a single pathological process based on the implementation of a hereditary factor under the influence of external and internal factors. Epigenetic factors include a family history of low birth weight and a high proportion of FGR in previous pregnancy (19.7 %) (OR – 3.11; 0.95 % CI: 1.68-5.75, p<0.001).

The proportion of patients with obesity/underweight was comparable and accounted for more than a quarter of the observations, which confirms the existing ideas about impaired fat metabolism and deficiency of nutrients and micronutrients in case of weight deficiency as a risk factor for placenta-associated pregnancy complications, including FGR (OR – 3.69; 0.95 % CI: 2.09-6.52, p<0.05) [4, 10, 15, 22].

A higher proportion of cardiovascular diseases (chronic arterial hypertension (17.1 %), gestational hypertension and preeclampsia (19.3 %), pelvic varicose veins (23.4 %)) found in the group with FGR also confirms the association with systemic endothelial dysfunction and its consequences – dysregulation of vascular tone and rheological disorders (OR – 16.32; 0.95 % CI: 2,25-118,57, p<0,05). A high proportion of anaemia compared with the control group (33.0% vs. 17.5 %, $\chi2=7.28$, p<0.01) should also be considered a pattern, which confirms the importance of this prognostic factor in the development of long-term hemic hypoxia in the intervillous space and impaired angiogenesis mechanisms (OR – 2.32; 0.95 % CI: 1.28-4.23, p<0.05). Whereas, placental dysfunction (47.6 %) with early pathological markers of uterine circulatory disorders according to Doppler is a local manifestation of changes in haemodynamics in the intervillous space, against which the risk of FGR increases 3-fold (OR – 3.12; 0.95 % CI: 1.81-5.40, p<0.05).

Assessing gynecological factors, it should be noted that the history of chronic pelvic inflammatory processes was more prevalent (60.9 % vs. 36.3%, $\chi2=16.74$, p<0.001), as well as carriage of cytomegalovirus infection (21.9 % vs. 11.3%, $\chi2=4.27$, p<0.05) and asymptomatic bacteriuria. Oligohydramnios was associated with impaired blood flow in the uteroplacental-fetal circulation in 127 obser-

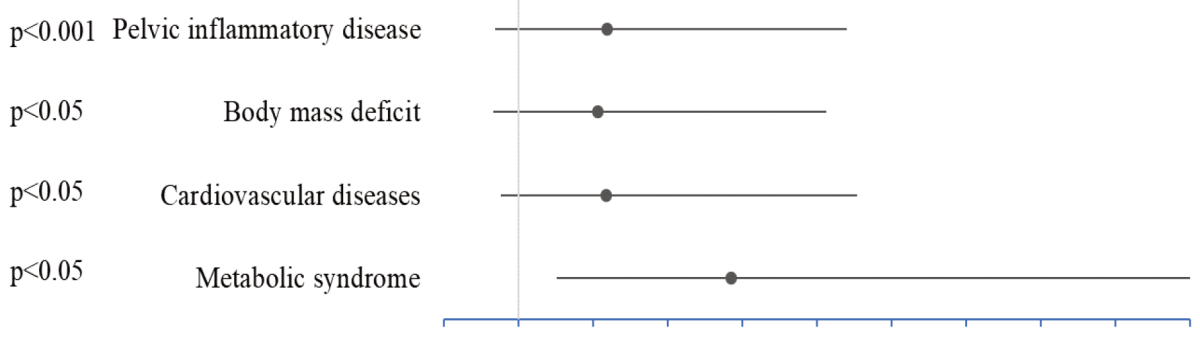

Figure 5. Forest plot of the odds ratio of the risk of fetal growth restriction by factors characterizing a woman's somatic health.

vations (19.4 %) versus 7 (8.8 %) in the control group ($\chi 2=4.75$, $p<0.03$).

At this stage, the most significant risk factors for the development of fetal growth restriction were identified, including: heredity and FGR in previous pregnancy (19.7 %) (OR – 3.11; 0.95 % CI: 1.68-5.75, p<0.001), socioeconomic factors and psycho-emotional cofounders (OR – 2.76; 0.95 % CI: 1.24-6.14, p<0.01), adverse lifestyle behaviours (smoking) (OR – 2.47; 0.95 % CI: 1.21-5.06, p<0.02), age over 35 years (OR – 2.82; 0.95 % CI: 1.74-4.57, p<0.05), multiple pregnancy (OR – 7.83; 0.95 % CI: 1.07-57.33, p<0.05), obesity or underweight (OR – 3.69; 0.95 % CI: 2.09-6.52, p<0.05), cardiovascular disease (OR – 16.32; 0.95 % CI: 2.25-118.57, p<0.05), anaemia (OR – 2.32; 0.95 % CI: 1.28-4.23, p<0.05), placental dysfunction (OR – 3.12; 0.95 % CI: 1.81-5.40, p<0.05), umbilical cord pathology and features of its insertion (OR – 3.77; 0.95 % CI: 1.61-8.82, p<0.05) (Figure 3).

As Table 1 shows, the division of the main group into two comparable groups – with early and late fetal growth restriction – allowed us to present a gradation of the leading predictors, taking into account the timing of the formation of FGR.

The age of women who gave birth to children with early FGR ranged from 19 to 42 years and averaged 33.6±2.4 years, the proportion of women who were pregnant and gave birth for the first time was higher (OR – 2.28; 0.95 % CI: 1.58-3.31, p<0.001). These data are in line with the generally accepted scientific positions of foreign and domestic medical communities regarding the increased risk of placenta-associated complications with the age of a woman [4, 6, 16, 14].

Studies of the role of epigenetic factors in the development of early and late FGR are controversial and few. Our observations show that in the presence of both low-weight and short-statured parents, every second child (62.4 %) is born with a weight low for gestational age without statistical differences between group [2, 3, 5].

There is a view that the success of pregnancy and its favourable course is associated with adequate mechanisms of implantation and placentation [4, 15, 16].

That is why factors of endometrial insufficiency, such as sexual infantilism and ovarian dysfunction (30.8 % and 15.3%, respectively, by group), uterine factors (uterine malformations, operated uterus) (42.8 % and 25.4 %), frequent instrumental interventions and chronic endometritis, infertility and the use of IVF programs, can be significant prognostic cofounders of the risk of early FGR (OR – 2.19; 0.95 % CI: 1.50-3.21, p<0.001) and placenta-associated complications in late pregnancy.

The assessment of the frequency of intrauterine instrumental interventions as a risk factor for endometrial dysfunction indicates a significant proportion of invasive operations (42.8 % and 41.6 %, respectively) without statistical differences in both groups (p>0.5). Significant deviations were demonstrated by the data on the number of non-developing pregnancies in the history and habitual miscarriage in the group with early FGR (16.4 % vs. 8.5 %, $\chi 2=6.88$, $p<0.01$). This pattern was confirmed in scientific studies reviewed during the literature search, where the authors presented the position that implantation and placentation disorders are the only pathogenesis of habitual miscarriage and gestational complications associated with placental dysfunction [4, 6, 16].

According to our study, the highest percentage of newborns with early FGR occurred in women with chronic arterial hypertension (28.3 %) and severe preeclampsia (35.8 %), acute respiratory infection during this pregnancy (37.1 % and 16.2 %, respectively), underweight at the pregestational stage (OR – 2.07; 0.95 % CI: 1.40-3.06, $p < 0.05$) and insufficient gestational weight gain (< 7 kg) (OR – 1.90; 0.95 % CI: 1.25-2.90, $p < 0.05$).

A comprehensive analytical review of the information obtained from 23,171 women's birth records and 598 patients who gave birth to children with FGR allowed us to gain insight into the groups and individual risk factors for early and late fetal growth restriction in the population of pregnant women in Kyiv and the region.

Depending on the degree of influence, the groups of factors were assigned ranking, where the most significant factors in terms of the risk of early FGR were the factors characterising the reproductive health of women and related to the course of pregnancy (Figure 4): sexual infantilism (OR – 2.46, 0.95 % CI: 1.61-3.76, p<0.05), uterine factor and infertility (OR – 2.19; 0.95 % CI: 1.50-3.21, p<0.001), first pregnancy in age over 35 years (OR – 2.28; 0.95 % CI: 1.58-3.31, p<0.001), spontaneous abortion and habitual miscarriage (OR – 2.11; 0.95 % CI: 1.23-3.62, p<0.001), instrumental intrauterine interventions (OR – 2.74; 0.95 % CI: 1.88-3.97, p<0.05), previous pregnancy with FGR (OR – 3.04; 0.95 % CI: 2.02-4.56, p<0.05).

In the complex of factors associated with the course of pregnancy, the largest proportion was gestational hypertension and preeclampsia (OR – 2.98; 0.95 % CI: 1.97-4.51, p<0.001), acute respiratory infections during this pregnancy (OR – 3.04; 0.95 % CI: 2.02-4.56, p<0.05), insufficient gestational weight gain during this pregnancy (< 7 kg) (OR – 1.90; 0.95 % CI: 1.25-2.90, p<0.05).

Next in the pyramid of ranks was the combination of factors characterizing a woman's somatic health (Figure 5), where the largest share made up chronic pelvic inflammatory diseases (OR – 2.19; 0.95 % CI: 1.50-3.21, p<0.001), underweight at the pregestational stage (OR – 2.07; 0.95 % CI: 1.40-3.06, p<0.05), chronic arterial hypertension and vascular disorders (OR – 2.18; 0.95 % CI: 1.41-3.36, p<0.05), and metabolic syndrome (OR-3.85; 0.95 % CI: 2.33-6.37, p<0.05).

The next group (Figure 6) included the so-called fetal and placental factors: placental dysfunction, repeated episodes of retrochorionic haematomas and pathological placentation (OR – 2.0; 0.95 % CI: 1.31-3.05, p<0.001), intrauterine infection (OR – 1.62; 0.95 % CI: 1.08-2.41, p<0.05), pathology of the umbilical cord and its insertion (OR – 3.04; 0.95 % CI: 2.02-4.56, p<0.05), fetal anomalies (OR – 2.20; 0.95 % CI: 1.16-4.17, p<0.05), which formed risk groups for both early and late FGR.

The influence of social factors in both groups related to psycho-traumatic factors of martial law, unstable financial situation due to lack of employment, and untimely medical examination and proper support due to migration circumstances remained signif-

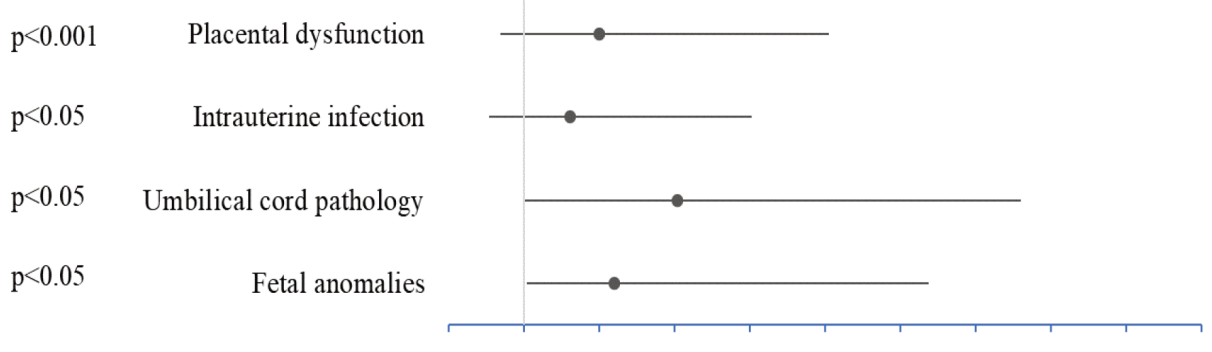

Figure 6. Forest plot of the odds ratio for the risk of early and late fetal growth restriction by factors characterising placental and fetal factors.

icant, which creates preconditions for the birth of low-birth-weight babies and confirms existing studies on the impact of social and domestic factors on the course of gestation [4]. However, social factors, bad habits, high levels of chronic stress and psychological trauma associated with martial law, internal and external migration, and the family's financial situation were an important predictor of FGR after 32 weeks of gestation (OR – 3.01; 0.95 % CI: 2.03-4.47, p<0.05).

Thus, fetal growth restriction as an obstetric syndrome arises as a result of combined mechanisms of fetal egg development and various mother's disorders, as a result of which microcirculatory changes in the structure, transport, endocrine, metabolic link with hemodynamic disorders in the "mother-placenta-fetus" system and the formation of placental dysfunction are generated [4, 14, 16, 22]. Fetal growth restriction as a consequence of multifactorial pathology is the result of the influence of medical-biological, social and environmental factors, the combination of which forms a clear prognostic assessment of the probability of developing this pathology.

Discussion

According to domestic and foreign authors, the main factors in the development of fetal growth restriction are the age of a woman under 17 years (young age) and over 35 years (late reproductive age), bad habits (smoking, alcohol, drug and toxin abuse) [14, 23, 24, 25], low body weight [2, 3, 5, 22], low socioeconomic status, extragenital diseases, infectious factors, sexual infantilism, habitual miscarriage and infertility [4, 6, 25]. Smoking during pregnancy is a leading and modifiable risk factor for fetal growth restriction and low birth weight (<10th centile), and higher Doppler resistance of the umbilical cord artery after 34 weeks of gestation [13, 23].

Among the medical and organisational factors, the authors identify the lack of pre-gravid training, defects in pregnancy management and non-compliance with standards in the management of high-risk pregnancies [24]. Gestational factors include induced pregnancies or the use of IVF programs, gestational complications (threatened abortion, hypertension or hypotension, anaemia, preeclampsia, gestational diabetes mellitus, multiple pregnancy, acute infectious processes during pregnancy) [4, 15, 22]. Feng Y. et al. indicate that important predictors of late onset of FGR were maternal height, weight, and medical history; mean arterial pressure in the first trimester; head-to-abdominal circumference ratio in the second trimester; and fetal weight estimate in the second trimester [15, 26, 27].

Alirzaieva Kh. in her works demonstrated the results of multivariate analysis, where in general the following factors had the strongest influence on the development of FGR: arterial hypertension (RR=2.055), obesity (RR=1.646), history of anaemia (RR=2.591), history of complicated labour (RR=1.886), habitual miscarriage (RR=1.850), history of preeclampsia (RR=1.922), and history of FGR (RR=3.502) [21, 22].

Among the chorionic and placental factors are placental dysfunction, premature placental abruption, heart attacks, premature placental maturation, single umbilical artery, umbilical cord insertion dystopia and other umbilical cord abnormalities [28, 29]. To date, it has been confirmed that the development of FGR from early pregnancy demonstrates an imbalance in the production of angiogenic factors and regulators of angiogenesis, and morphological findings in the study of the placenta demonstrate evidence of inflammatory alteration and tissue ischemia [13, 16].

Given the long-term pandemic of COVID infection, many authors have expanded their scientific research to assess the impact of the COVID-19 virus on the vascular system of the uteroplacental locus and have established that morphofunctional changes in the chorion/placenta in pregnant women with

COVID-19 against the background of post-COVID endotheliitis are the main pathogenetic factor in the development of preeclampsia, FGR, antenatal fetal death, and impaired fetal and neonatal condition [30, 31, 32]. In placental tissues during pregnancy with COVID-19, a team of scientists found an increased prevalence of decidual arteriopathy and other signs of maternal vascular hypoperfusion, which causes oxygenation abnormalities and leads to adverse perinatal outcomes. These changes may indicate complications associated with placental viral infection, systemic inflammation (cytokine storm), maternal hypoxia, or hypercoagulability [16, 30, 32].

Fetal factors are represented by aneuploidies, gene and chromosomal aberrations (trisomies 13, 18, 21), fetal malformations and congenital infections, metabolic defects, etc. Although these factors have not yet been systematized, their share and specific weight in the structure of factors for the formation of early and late fetal growth restriction has not been determined [6, 7, 16].

It should be noted that FGR is often underdiagnosed, which led to a missed diagnosis in 11.5 % of infants. The authors explain this fact by the incorrect use of the screening method in clinical practice and suggest rethinking the time and frequency of scheduled third-trimester ultrasound [24].

That is why the introduction of modern prognostic algorithms, unified diagnostic criteria and principles of management of pregnancy with FGR into daily clinical practice is the basis for reducing perinatal mortality and morbidity.

Conclusions

Clinical and social risk factors for fetal growth restriction include the status of temporarily displaced persons and a significant proportion of psycho-traumatic factors, a high index of somatic diseases and impaired reproductive health. There is no doubt about the role of infection in the genesis of FGR, which demonstrates a high proportion of gynecological diseases, chronic endometritis, and pelvic inflammatory diseases, where, on the one hand, FGR is a leading symptom of intrauterine infection and a predictor of antenatal infection. The age group was represented by first-time mothers over the age of 30, and every fifth patient was underweight. Habitual miscarriage, frequent episodes of retrochorionic haematomas, and gestational complications (preeclampsia, placental dysfunction, and threatened abortion) should be noted. When analysing fetal factors, attention should be paid to multiple pregnancies, fetal malformations, etc. Among the placental risk factors, pathological placentation, placental dysfunction, and umbilical cord pathology (umbilical cord insertion abnormalities, two umbilical cord vessels, and Wharton's jelly hypoplasia) dominate, which, along with structural placental abnormalities, contributed to a decrease in metabolic area and impaired blood flow. Factors associated with reproductive health disorders and complicated pregnancy are important in the development of early fetal growth restriction, while fetal and placental factors are equally important predictors of both early and late forms of this syndrome.

Thus, it is indisputable that the range of factors leading to the development of fetal growth restriction is quite wide and multifaceted, which requires the development of prognostic models, preventive approaches and a program of careful dynamic monitoring and rational decision.

Participation consent

Written information consent was obtained from the patients.

Data availability

Further data are available from the corresponding

author on reasonable request.

Conflict of interest

The authors declare no conflict of interest.

Article publication

The authors declare that the materials presented in the article are original and have not been previously published or submitted for publishing.

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