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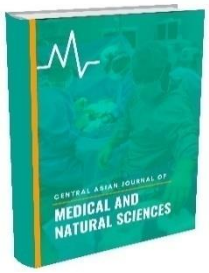

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Modern Aspects of the Problem of Fetal Growth Restriction Syndrome and Methods of its Correction

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Abstract: **1.1. Modern perceptions of fetal growth restriction syndrome and its prevalence.** Fetal growth restriction syndrome (FGRS) is considered one of the most pressing problems in modern obstetric theory and practice and occupies a significant place in the structure of perinatal diseases and cases of death. FGRS, according to researchers in our country, occurs at a frequency of 5 to 22% among babies born during their term, and in premature babies – from 18 to 24%. According to the World Health Organization, the number of newborns with symptoms of height development reaches 6.5% in Europe and 31% in the regions of Central Asia. In the United States, enemas are diagnosed in 10-15% of cases in newborns, in 30% of cases it is noted that the fetus lacks oxygen during ejaculation, while in Russia these indicators are up to 2.4-17% [2.5.7]..

Fetal growth restriction syndrome in the Republic of Uzbekistan is recorded in 4.1-20.0% of cases [10].

M. I. Ismatova (2017) based on results from a retro-and prospective study for 2014 at the Perinatal Center of the Bukhara region, found that the number of babies born with fetal growth restriction syndrome at gestational age was 37 or more, with 73 out of 3,476 children born during their term having fetal growth restriction syndrome, which is 5.1% [3].

Babies born with enemas are observed to develop physically and mentally at a small rate, which is observed with high somatic and Infectious Diseases [7]. Children born with enemas before school age maintain deviations in neurological status, the expression of pathology of the central nervous system is due to the level of enemas and the influence of intrauterine hypoxia symptoms of the fetus [12]. In the last decade, the hypothesis of "fetal programming" in medicine is widely discussed, according to which the health of children is related to the conditions of development within the uterus [17].

Among stillborn babies, 20-50% had oxen. Perinatal mortality was 3-10 times higher in FGRS patients and disease susceptibility was 2-8 times higher than average in the first 12 months of infant life [I. Bernstein, 2011]. A complication of prolonged fetal ischemia in the presence of FGRS is a violation of adaptation in the postnatal period, the result of which leads to hypersensitivity, resulting in a delay in physical, somatic and neuropsychic Development [20].

By extension, in modern foreign literature, the terms "asymmetry" and "hypoplasty" are used instead of the concept of "hypotrophic form of AIDS". The term "symmetry" replaced the concept of "dysplasty". [12]. In our country, Obstetricians, neonatologists, ultrasound diagnostic doctors simultaneously speak different languages, using the concepts: "fetal lag in development within the uterus", "fetal growth restriction syndrome", "intrauterine hypotrophy", "low body weight fetus", "fetal lag syndrome in development within the uterus", "syndrome that manifests the result of a complex polycausal reaction of the fetus and patients formed in different pathological conditions of the mother's organism". [2] The most important of these is" fetal lagging in growth", since it is impossible to conclude whether the fetus is lagging in development only on the basis of indicators of body weight and height [18].

According to bsst recommendations in 1961, newborns with a body weight of less than 2,500 G are children with a low body weight at birth. INTERGROWTH-21st measurement is used depending on gestational age (24-42 weeks). If the body weight and/or length is below 10-percentile, the child is diagnosed with fetal limb retardation syndrome and, according to XKT-10, has a gestational age of underweight (lower body weight values) (p05.0 category); is younger than gestational age (lower weight and length values) (p05. 1 category); the diagnosis of inadequate fetal nutrition (P05.2 category) is established [5].

As a result, FGRS is a problem that requires attention in the Perinatology Department. This disease affects not only the development within the mother, but also the postpartum period. The more complex the enemas, the more pathologies the existing child-placenta-fetus has in the cardiovascular system, thus having an even greater impact on the child's postpartum development. In children, it often becomes necessary to maintain medical supervision for a long time, in most cases to correct with drugs, and, if necessary, to invite a large number of specialists (neuropathologists, orthopedists, immunologists). Due to the development of modern technologies and early diagnosis, the number of complications in the development and birth of the fetus has significantly decreased.

1.2. Risk factors and development theory of fetal growth delimitation syndrome. Modern discoveries in Perinatology have identified new unresolved problems in the field of fetal pregnancy process and antenatal protection. One of the most common pathologies is placental dysfunction, which occurs in 14-22% of cases, it is also worth noting the lack of fetal oxygen and stunted growth, which are the most common (60%) cause of death in the perinatal period. Due to the development of modern technologies and scientific projects carried out in our country and in the world as a whole, the incidence of death in the diagnosis of the symptom of fetal growth delimitation decreased significantly, but the prevalence of this pathology in the perinatal period remained unchanged [4; 18.].

Therefore, to this day, the search for new ways of early diagnosis of placental insufficiency has been one of the most promising areas.

A.N. Strijakova and et. all (2015) found that large numbers of changes occur in the child's body in the formation of the enema, which are the cause of disorders in the child's physical and mental development in the early years of life, as well as high somatic and Infectious Diseases [6].

To date, there is no reliable theory of the appearance of enemas. Therefore, this pathology is polyethiological. Every year there is an increasing need to study the causes of this disease, but the etiology of many of them remains unknown. Risk factors are also very broad.

To date, the causes of enemas are divided into 4 types: maternal-related, fetal-related, intrauterine, placentar Factor [8.16]. In the study of enemas, the mother's factor attracts the most attention. These facts: features of body constitutionality (low weight before pregnancy) age of the mother, up to 18 years and over 35 years: socio-economic reasons: include the presence of chronic intoxication

(nicotine, drugs, alcohol) [10]; includes living in areas with adverse conditions where there is air pollution [12].

The peculiarities of geography and climate in the area where the pregnant woman lives also lead to the development of enemas. Thus, chronic hypoxia in women living in high mountain areas can reduce placentar perfusion, which leads to the development of enemas [13].

I. V. Barinova believes that the development of placental insufficiency occurs against the background of external influences on the body that lead to hemodynamic disorders, gas exchange of the fetus and the mother, as a result of which there are changes, with the development of the enema, a negative result of the perinatal period is observed [14].

Optimal pregnant nutrition is the basis for the healthy development and growth of the fetus; experiments carried out within the framework of various laboratory studies (experiments on animals) have repeatedly proved this. [12; 16].

Extragenital diseases of the mother can negatively affect the fetus. Often chronic diseases are the background of the development of pregnancy complications that lead to hemodynamic disorders in the mother's body, including the pool of the uterine artery [22].

R. According to Romero (2008), hypoction developing in PE can control PlGF expression in placentar tissue to increase the formation of sflt-1, which in turn can competitively bind VEGF and PlGF free circularizing proangiogenic factors as well as make the state more severe by tilting the balance towards the antiangiogenic State [10].

Endothelial disorders occur in pregnant patients at the stage of chronic pathology of the kidneys and genital tract, and the production of many peptides and proteins during the acute course of the disease is impaired [17]. These facts affect hemostasis, increased coagulation, placental insufficiency, which leads to the development of enemas [14.]. Animal studies prove that pregnant women with cardiovascular and respiratory diseases live in low-oxygen areas. [21].

E.V. Volkov, Yu.V. Kopylov's (2014) work found the role of proangiogenic (PIGF) and antiangiogenic stem factors in the pathogenesis of placental insufficiency and fetal lagging in 116 women with FGRS. The results found reliable differences in the level of vascular factors of growth in blood plasma in patients late with pregnancy placentar insufficiency as well as with enemas, compared with healthy pregnant women. Compared to healthy pregnant women, the level of proangiogenic vascular factor was significantly lower in patients with FGRS, at which time the level of antiangiogenic vascular factors was reliably higher in pregnant women with FGRS, compared to the data of women in the control group. When PE occurs and the incidence of nausea varies from mild to moderate to severe, compared to healthy pregnant women, the placentar growth factor decreases by 1.5, 6 and 11.5 times, respectively; there is an increase in sFlt-1 in 5, 7 and 9.8 times, respectively, and an increase in soluble endoglin in 2 or more. the antiogenic coefficient (ka) calculated by the formula s-Flt/PlGF×10 has increased dramatically in the Ox-weighted state [26].

M.Ya Kamilova, D.M. According to rakhmatullaeva (2015), the specifics and Risk Factors of PE development in modern conditions of Tajikistan have been studied. In 2014, Tajikistan AG and

A retrospective analysis of the medical history of 2,907 pregnant women admitted to the Piti pregnant women pathology unit was conducted. Thus, among women admitted to the clinic'S HAPB, PE was identified in 1,527 women, representing 52.5%. The highest frequency of PE development was found in succulent pregnant women (82.4%), preeclampsia (67.8%), as well as in pregnant women with anemia (70.5%) [26].

All of the above affects different periods of pregnancy, which leads to the assumption of several factors for the appearance of enemas. At the moment, we have many versions of the development of FGRS, but there are several more related versions.

According to one of the theories, as a result of a decrease in the number of cells during pregnancy, their next number is not restored, and a fetometric decrease in fetal indicators develops against this background [9; 25].

The main theory in the pathogenesis of the appearance of foci is the hemodynamic dysfunction of macro-and microtomirs due to changes in pressure in the placenta and vessels [9,11]. in parallel with the development of trophoblast insufficiency, blood circulation decreases. Smooth muscle tissue and adrenergic tissue maintain their ability on the placental side, and as a result, placental vessels react to vasoconstrictors, leading to dysfunction of the placental circulation [3.15].

Many studies have noted that changes in immune control mechanisms lie in the gestational process based on impaired maternal-placental-fetal system function in FGRS [17]. There may be a violation of the defense mechanisms against trophoblast apoptosis, since the mechanisms of apoptosis are regulated by proinflammation and cytokines of inflammation. The development of blood vessels in the placenta as a result of apoptosis is observed due to the presence of angiogenesis and vasculogenesis. They undergo active apoptosis, as a result of which restriction in the nutrition of trophoblasts develops, and as a result, placental insufficiency develops [5; 18].

P.L. Mileeva (2020) Moscow sh. in " V.N. On the basis of the federal state budgetary institution" Research Institute of motherhood and childhood named after Gorodkova " carried out a comprehensive examination in 209 women with enemas. The characteristics of somatic and obstetric-gynecological Anamnesis were analyzed in patients with poor fetal growth and development. Smoking increases the likelihood of fetal growth retardation (OR=1.91), diagnosis of extragenital diseases (chronic pyelonephritis (0r= 2.04)), thyroid disease (0r = 2.00), or increased (or= 1.86), and decreased blood pressure (0r = 1.53), which is complicated by intrauterine problems (uterine fibroids (0r = 2.06), fetal growth retardation syndrome in previous births (0r = 1.86), early pregnancy tuxtashi (0r = 1.8), abortions according to medical (0r = 1.75) guidelines prior to the current pregnancy [19].

1.3. The role of gene polymorphism in the pathogenesis of the development of fetal growth restriction syndrome. Thanks to the study of the human genome in the next decade, scientists have managed to identify a number of genes responsible for obstetric pathologies. Also, these discoveries made a forecast of the presence and occurrence of obstetric diseases [13; 23].

It is worth noting that FGRS is a syndrome caused by a number of pathogenic factors, rather than an independent classificable cassality. Placental insufficiency is one such factor that causes difficulties in the course of pregnancy.

According to obstetric practice statistics, fetal deaths in Ox are 7.5-10 times more common than in cases of fetal deaths not conditioned by any patalogies. This, in turn, is due to the fact that pathogenic factors that cause enemas directly cause fetal death.

A characteristic feature of placentar deficiency is that it is a "continuation", "cause"of enzymatic deficiency in the placentar shell. Structural changes in the placenta also weaken its regenerative characteristics. Placental insufficiency can also lead to fetal hypoxia and blood deficiency. While uterine patalogies account for 40% of placentar deficiency cases, it has not yet been determined for what cause or factors the remaining cases occur.

Some markers, separated by molecular genetic analysis, may be the causes of pathologies in which they are responsible for protein synthesis and various mutations.

Over the past years, a wide range of genes associated with the development of the Pheto-mother complex have been studied, including genes controlling the immune system response in implantation and placentation processes (IL10, IL6, IL6R), vascular network formation in the placenta (VEGFA), controlling the metabolic function of the placenta (PPARG, IGF II), as well as genes leading to disruption of the blood clotting system (F2, F5, FGB, ITGA2, itgb3, SERPINE1), formation of vascular networks in the placenta (VEGFA), the genes that control the metabolic function of the placenta (PPARG, IGF II, PLA 1, PLA2), as well as causing disruption of the blood coagulation system (F2, F5, FGB, ITGA2, ITGB3, SERPINE1) were most studied [12].

One of the main directions in medicine is the identification of the molecular-genetic aspects of the disease. The gene is part of a deoxyribonucleic acid (DNA) molecule that has a nucleotide sequence that determines the mechanism of protein synthesis. Genes present in several different species - alleles-in populasia are called polymorphic genes, causing the characters to be different within the species. Genetic diversity is largely based on single nucleotide migration and variation in the number of repeat DNA fragments in the genome [10;15]. The prevalence of certain polymorphic variants of genes may be associated with the development of a complication of pregnancy (usually premature delivery, hypertensive disorders of pregnancy) [22; 24].

There are studies showing that hereditary predisposition to thrombophilia is associated with a higher risk of pregnancy-induced copulation (early termination of pregnancy in early terms, placentar insufficiency, enemas and preeclampsia) [15].

A group of Uzbek scientists (Boboev K.T., Mavlyanova N.N., Ibragimov Z.Z. (2017)) studied allele variants as well as genotype polymorphism in the NOS3 gene rs1799983 G/T gene in pregnant women with fetal growth retardation syndrome. The results obtained show that the dependence of the NOS3 gene rs1799983 on polymorphism in pregnant women has no predictive significance in the development of fetal growth retardation syndrome, which has no reliable character ($p>0.05$) [10.].

Hemostasis dysfunction and heredity play an important role in the pathogenesis of hocs [4]. To date, many factors have been studied that influence the development of thrombus complications [6.16]. The active form of Factor V acquires a sparse character in the presence of a Leisgenovsky mutation. The protein tolerance (resistance) of the S-reagent has developed, as a result of which there is an increased risk of large aggregation as well as the occurrence of cases of thrombosis. [5.19].

In cases of methylentetrahydrofolateductase (MTGFR) deficiency, the inner wall of the vessels is damaged. Such quantitative indicators of MTGFR, in turn, cause thromboses and impaired function of the inner walls of the vessels. [9; 12].

Dugalich argues that the observation of a gene (RA1-1) that slows down the process of cleavage of the enzyme plasmin precedes the process of polyformism. In addition, this gene is a characteristic sign that an inflammatory process is going on in the body, which leads to damage to the outer shell of the fetus. As a result of this, there is a risk of the origin of hocs. The homozygous form of the Ra1-1 gene, 675 4G/4G, is considered to refer to the birth of sogbola.

The diversity of platelet receptors, which play a role in controlling secondary stages of bleeding cessation, leads to fibrinogen formation, which binds to platelet receptors, causing the formation of quae and the deposition of blood plates [17; 23]. These scientific works expand the possibilities of understanding the mechanism of pathogenetic conditions in many areas, including obstetrics. Currently, research into the diversity of responsible genes is gaining popularity. Most polymorphic sites at different sites of Tsitokin genes have been studied [23;29]. Polymorphisms associated with point mutation changes in which exons and introns are localized are most likely to be characterized. The structure and functions of molecular peptides are disrupted by changes in gene exons. Polymorphic variants in the promoter region of the gene typically control gene activation [25].

Variants of polymorphic gene introns are very common in population. The activity of allelic peptide molecules in intron parts of genes may be affected by changes [15]. The structure of the promoter (control) parts of genes is now widely studied [19]. In general, the exchange of single nucleotides in DNA molecules indicates cases of polymorphism. This process was studied within the framework of a number of classes, the degree of its involvement in one or another pathalogy was assessed. [16; 23.]

Newman [13; 17] a 2008 study found that the IGF 2 gene encoding IGF2 synthesis causes fetal growth in mice, at which point the IGF2R gene encoding the IGF2R receptor may delay fetal development within the uterus. The maternal gene H19, which controls the expression of the IGF2 gene, is of great importance for weight control after birth. The H19 + 2992 variant is compatible with increased IGF2 concentration and controls fetal growth [11.18]. In fetuses late in development inside the uterus, there is not only a decrease in insulin-like growth factors, namely the concentration of IGF1 and IGF2, but also a decrease in the concentration of IGF1-binding proteins. Positive correlation between IGFBP3 levels (protein that binds the insulin-like growth factor) and negative correlation between IGFBP1 levels and body weight at birth have been documented [12; 25].

Positive correlations of leptin and insulin levels as well as IGF1 and IGFBP3 levels have been found in existing fetuses [130; 69 b]. Maternal genes play an important role in the regulation of fetal growth: PHLDA2 (a member of the plextrine homologous domain Family A) is involved in the regulation of placental growth, GRB10 (growth receptor binding protein) – this protein is responsible for signaling. The Insulin receptor as well as the IGF1 receptor signal [132; 89 b] as well as the placentar ALS quench (acidic subunit), the IGF1-binding protein responsible for its Half-Life [25; 34].

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