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Mini Review

Modern Etiopathogenetic Concepts of Fetal Developmental Anomalies

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Abstract

This article provides an analysis of literature data on the etiopathogenetic aspects of fetal developmental anomalies in women, taking into account the leading risk factors. Despite the wide knowledge of etiological aspects, the development of diagnostic strategies and prediction methods, the incidence of fetal developmental anomalies does not show a tendency to decrease, remaining a major medical and social issue.

Keywords: Fetal developmental anomaly, Chromosomal abnormality, Congenital anomaly, Genetics

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Currently, up to 5% of newborns are born with various congenital and hereditary disorders. About 30% of pediatric inpatient beds are occupied by children with hereditary pathology, and up to 40% of infant mortality is associated with hereditary and congenital defects. In this regard, prenatal diagnosis—particularly the development of methods for early detection of congenital anomalies and hereditary diseases of the fetus—has great importance. Advances in ultrasound scanner quality, the ability for digital image processing, and especially the implementation of high-resolution transvaginal sonography have enabled a shift in the prenatal diagnostics of hereditary and congenital disorders to the first trimester of pregnancy [1-9]. Congenital malformations or developmental anomalies represent deviations from the normal anatomical structure of the body that occur in utero as a result of impaired development during embryonic or fetal periods, and less commonly after birth due to disruption of organ morphogenesis [1,10,3,4]. Congenital anomalies may arise under the influence of single or combined environmental and genetic teratogenic factors affecting normal embryo or fetal development [11]. According to various authors, in 50–70% of cases the causative factors remain undetermined [12,3].

Approximately 20% of anomalies have a multifactorial etiology; the contribution of genetic factors (gene mutations and chromosomal abnormalities) accounts for about 6%. A smaller proportion is linked to maternal infections (2–3%), diabetes (1.5%), other diseases (less than 1.5%), and medication exposure (1–2%). Congenital limb anomalies may occur in isolation or in combination with defects in other organ systems [5,6]. They more frequently affect the lower limbs, accounting for 55% of all musculoskeletal congenital anomalies [7]. However, U.S. statistics show a higher incidence of upper-limb reduction defects compared to lower-limb anomalies [8,13,14,15].

While second-trimester fetal anomaly scanning is considered routine and efficient, ultrasound examinations in early pregnancy still require further methodological refinement [14]. Discussion continues regarding the efficiency and economic feasibility of first-trimester ultrasound screening. According to a 2021 Cochrane review, early screening in 4 million pregnancies in the U.S. increases national healthcare costs by approximately $1 billion annually [4,8,16,13,17]. Current national guidelines specify that the primary goal of the first-trimester (10–14 weeks) screening ultrasound is the assessment of nuchal translucency to form a high-risk group for congenital and hereditary disorders. Detailed assessment of fetal anatomy is not mandated in the protocol [13,18-21,14]. Substantial international and domestic experience has been accumulated regarding the detection of anomalies by sonography at the end of the first and beginning of the second trimester. Significant detection rates have been demonstrated only for severe and major anomalies [11]. Most anomalies are still diagnosed in the second half of pregnancy.

The low efficiency of early prenatal ultrasound diagnostics is mainly linked to the lack of a unified protocol for structural assessment during first-trimester screening. Moreover, the actual diagnostic capability of prenatal ultrasonography in early pregnancy remains insufficiently studied. This research was designed to address these gaps within a prenatal diagnostic center performing both screening and consultation-based scans. [2,11,21,15,9]. Global statistics show similar rates of congenital limb anomalies: 3.44 per 10,000 in England, 5.45 in Italy, and 4.79 in Brazil [11,13,15]. Thus, the incidence does not significantly differ across various populations. Prenatal detection of congenital and hereditary disorders continues to be a major challenge in perinatal medicine. Despite scientific advances, widespread ultrasonography, and the introduction of screening programs, the number of children born with congenital pathology remains high. Many of these children become disabled or die [2-6,22,19]. Chromosomal abnormalities are among the most common congenital and hereditary disorders, with an incidence of 7–8 per 1,000 liveborn infants. Severe chromosomal defects occur in 2–3 per 1,000 births and are incompatible with life or health [2]. Despite the availability of cytogenetic testing methods during pregnancy, the frequency of chromosomal syndromes among newborns has not decreased [10,18,21].

Improving prenatal detection of chromosomal abnormalities is therefore crucial not only for clinical medicine but also for national health priorities [1,19,14]. Although the risk increases in women ≥35 years and families with adverse reproductive history, 70–80% of chromosomal anomalies arise as de novo mutations in younger, low-risk parents [13,18,14]. Thus, effective prevention is limited and early diagnostic approaches must be optimized. Chromosomal defects often manifest as diverse ultrasound findings—from major structural anomalies to minor "soft markers" not affecting anatomy. Most abnormalities are recognized during the second trimester [1,3,5,8]. Significant worldwide progress has been achieved in identifying ultrasound markers of chromosomal aberrations over the past two decades. However, in our region, insufficient fundamental research exists on this topic, despite increasing clinical focus on chromosomal diagnostics. The current second-trimester ultrasound screening protocol does not mandate evaluation of ultrasound markers of chromosomal anomalies. The absence of a standardized marker list, diagnostic criteria, optimal timing, and further clinical management recommendations reduces detection accuracy and negatively affects perinatal outcomes [1,11,4,6,18,20]. Congenital Heart Defects (CHD) are among the most common anomalies, occurring in 7–12 per 1,000 live births [2,7,16,13,14,23,24]. All the above indicates the necessity of further research on second-trimester ultrasound markers of chromosomal pathology to improve comprehensive prenatal diagnostics and enable timely decision-making regarding pregnancy management.

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Conflict of Interest

None.

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