Modern data on factors determining the formation of congenital heart defects in children

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Abstract: In modern conditions, the health of newborns and their further development are influenced by biological, social and environmental risk factors of the perinatal period: poor health of parents, especially the mother; poor nutrition; an increase in the number of families at high medical and social risk; deterioration of the quality of the environment. In the first year of life, biological factors have the greatest impact, so in total they amounted to 82.4% in the first year of life, 62.8%> - in the second year, and 13.1%> - in the third year of life. Among them, the most significant are the health of the parents, the course of pregnancy and childbirth, the degree of full-term pregnancy, the duration of breastfeeding, etc. In this regard, the issue of studying clinical and diagnostic criteria for improving the provision of timely medical care to children with congenital heart disease at an early age remains relevant and requires scientific research in this area.

Keywords: congenital heart defect, malformations, etiology, anomaly, defect

Congenital heart defects (CHD) consist of a wide range of anomalies and malformations affecting the heart and great vessels that develop in utero, are present at birth, and present in infancy, adolescence, or adulthood. Cardiovascular anomalies typically result from defective morphogenesis during embryologic development. Malformations may be limited to the cardiovascular system (nonsyndromic) or occur in combination with anomalies of other systems as part of specific syndromes (syndromic).

The most common CHDs diagnosed in infancy are muscular and perimembranous ventricular septal defects followed by secundum atrial septal defects, with a combined prevalence of 48.4 cases per 10,000 live births.

Approximately 85% of children have a multifactorial etiology of CHD in children, which is usually the only malformation in the child and is the result of the interaction of many individually undefined genes and a number of other causes. The risk of recurrence of CHD in a family varies depending on the cause. The risk is negligible for de novo mutations, 2–5% for nonsyndromic multifactorial CHD, and 50% for cases

where the cause is an autosomal dominant mutation. It is important to identify genetic factors, as most patients with CHD survive to adulthood and potentially start families.

Anomalies in the anatomical development of the heart and large vessels usually form during the 2nd to 8th week of intrauterine development as a result of impaired embryonic morphogenesis and can be caused by both hereditary (gene, chromosomal, genomic, zygotic mutations) and environmental factors affecting the developing embryo. The specific causes of congenital heart disease are unknown. Most often, congenital heart disease is sporadic, not associated with a syndrome, and of unclear etiology. Genetic etiology has not been identified in approximately 72% of patients with congenital heart disease. They are often associated with chromosomal abnormalities detected by karyotyping in more than 1/3 of patients with congenital heart disease. Most often, it is trisomy of chromosomes 21, 18 and 13. In addition to Down syndrome, there are about 20 hereditary syndromes, in most cases accompanied by congenital heart disease. In total, syndromic pathology is detected in 6-36% of patients. However, some of these anomalies account for only about 5-6% of patients with congenital heart disease. The monogenic nature of congenital heart disease has been proven in 8% of cases; about 90% are inherited multifactorially, i.e. they are the result of a combination of genetic predisposition and the impact of environmental factors. The latter act as provoking factors, revealing hereditary predisposition when the "threshold" of their combined action is exceeded. The risk of recurrence of congenital heart disease in a family varies depending on the cause. The risk is insignificant for newly emerged mutations, 2-5% for non-syndromic multifactorial congenital heart disease, and 50% when the cause is an autosomal dominant mutation. Genetic code defects and embryogenesis disorders can also be acquired: exposure of the fetus and mother's body to certain unfavorable factors (radiation, alcoholism, drug addiction), endocrine diseases (diabetes mellitus, rubella, systemic lupus erythematosus, thyrotoxicosis), viral and other infections suffered in the first trimester of pregnancy (rubella, influenza, hepatitis B), intake of medications (lithium preparations, warfarin, thalidomide, antimetabolites, anticonvulsants, lithium, isotretinoin, anticonvulsants). Mixed viral and enterovirus infections suffered by the fetus in utero are of great importance in the development of cardiac and vascular pathology. In addition to etiological factors, there are risk factors for the birth of a child with congenital heart disease. These include: maternal age; toxicosis and threat of termination of the first trimester of pregnancy; history of stillbirths; presence of children with congenital malformations in close relatives. It is unclear whether maternal age is an independent risk factor for the development of CHD. Paternal age may also be a risk factor.

The impact of unfavorable factors on a woman can disrupt the differentiation of the heart and lead to the formation of congenital heart disease. Such factors are considered to be:

• infectious agents (cytomegalovirus, herpes simplex virus, influenza virus, enterovirus, Coxsackie B virus, etc.);

• hereditary factors - in 57% of cases, congenital heart disease is caused by genetic disorders, which can occur both in isolation and as part of multiple congenital malformations; the most well-known causes of congenital heart disease are point gene changes or chromosomal mutations in the form of deletion or duplication of DNA segments;

• somatic diseases of the mother, and primarily diabetes mellitus - lead to the development of hypertrophic cardiomyopathy and congenital heart disease;

• professional hazards and bad habits of the mother (chronic alcoholism, computer radiation, mercury and lead intoxication, exposure to ionizing radiation, etc.).

The most common defects are: ventricular septal defect - VSD (28.3%); atrial septal defect - ASD (10.3%); pulmonary artery stenosis (9.8%); tetralogy of Fallot - TO (9.7%); aortic stenosis (7.1%); coarctation of the aorta - PA (5.1%); transposition of the great vessels (4.9%); hypoplastic tricuspid valve syndrome, patent ductus arteriosus (PDA), and complete anomalous venous return are also encountered.

Intrauterine infectious pathology of the fetus and newborn is one of the most pressing and complex problems in pediatrics. The proportion of infectious and inflammatory processes in the structure of perinatal mortality is about 10-18%, second only to intrauterine asphyxia, respiratory disorders, and congenital anomalies. The relevance of the problem of intrauterine infection is due not only to significant peri- and postnatal losses, but also to the fact that children who have suffered a severe form of congenital infection very often develop serious health problems, leading to disability and a decrease in the quality of life in general.

Among the pathogens, a special position is occupied by TORCH-complex infections - Toxoplasma (toxoplasmosis), Rubella (rubella), Cytomegalovirus (cytomegalovirus), Herpes (herpes). Includes such infections as hepatitis B and C, syphilis, chlamydia, gonococcal infection, HIV infection, listeriosis, enterovirus infection and others affecting the fetus.

In the absence of adequate therapy during pregnancy, up to 50% of newborns with at least one TORCH infection in the mother are born with various injuries: intrauterine infections (IUI), intrauterine growth retardation (IUGR), hypotrophy, expected malformation (EM), including congenital heart disease, cerebrovascular accidents. In mixed infections, the incidence rate in newborns reaches 50-100%.

In the studies of Lobzova A.V. (2014), immunological markers for a particular infection or association of infectious agents were diagnosed in newborns with and

without congenital defects. In this case, class G antibodies to viral-viral associations (CMV + herpes simplex virus (HSV)) were frequently determined both in the main and control groups (56.33 and 65.38%, respectively). In the main group, class G immunoglobulins to HSV were detected in 98.6% of the examined newborns and in 80.7% of children in the control group, to CMV - in 95.8 and 96.1%, respectively, which is consistent with the literature data on the ever-increasing incidence of these pathogens in the population.

Due to the fact that the frequency of intrauterine infections does not tend to decrease and, accordingly, there are no adverse consequences, further study in this area is required to develop measures to prevent them.

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