FREQUENCY AND STRUCTURE OF CONGENITAL MALFORMATIONS IN THE REPUBLIC OF KARAKALPAKSTAN FOR THE PERIOD 2020-2025

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Abstract. *The aim of the study is to analyze the frequency and structure of congenital malformations (CM) in the Republic of Karakalpakstan for 2020–2025.*

Official regional monitoring data was used as source material. The results showed that the level of CHDs ranged from 129 cases in 2020 to 200 cases in 2024. The structure was dominated by congenital heart defects, Down syndrome, and cleft lip and palate. The data obtained underscore the need for further development of the prenatal diagnosis system, increased accessibility of screening technologies, and a comprehensive approach to the prevention of congenital malformations. Strengthening monitoring and conducting additional epidemiological studies will not only clarify the true extent of the problem, but also help to develop effective measures.

Keywords: *congenital malformations, epidemiology, Karakalpakstan, newborns.*

Congenital malformations (CM) in children are among the leading medical and social problems in the modern world every year [1,2].

Fetal malformations are one of the most dangerous complications leading to disability and mortality in fetuses and newborns. They rank second or third among the causes of perinatal death in fetuses and newborns [2].

In every third case (25-30%) of perinatal loss, anatomical defects of various organs and systems are found, and in every fourth case (25%), the death of children in their first year of life is caused by fetal malformations [2, 3].

According to WHO data, 4-6% of children born worldwide each year have CHD, and 40% of them die. On average, 2.5-4.5% of CHD cases are detected immediately after birth, and another 5% of disorders are detected during the first year of life [4].

For more than 30 years, Europe has had a single European registry for congenital malformations and fetal development anomalies – the European Surveillance of Congenital Anomalies (EUROCAT). According to the registry, 1.7 million children with developmental defects are born worldwide each year, with one in ten of them in the European Union [5,9,10].

Research by Russian scientists has shown that the incidence of CHD in Russia ranges from 3% to 7% depending on the region: in 15% of cases, defects incompatible with life are recorded, and in 2% of cases, severe anomalies are recorded [6]. In premature babies, the overall incidence of CHD is three times higher than in full-term babies – 33.2% and 10.9%, respectively [6,8].

Research by Akhmedov M.E. showed that congenital heart and circulatory defects account for almost one-third of the structure of CHD among children in the Republic of Uzbekistan as a whole [6,8].

It should be noted that not all malformations are detected at the time of birth. Some are detected later: by the age of two, anomalies are diagnosed in 6% of children, by the age of five in 8% of children, and 2% are diagnosed in older children [4, 5, 13]. Currently, the prevention of congenital

diseases in the fetus is divided into primary and secondary prevention. Primary prevention is aimed at improving the environment and taking a number of measures to improve the health of parents before and during pregnancy [6, 7,11]. Improving antenatal diagnostic methods, screening pregnant women for the presence of VPR, and introducing modern perinatal technologies are the main conditions for reducing perinatal mortality [5, 8, 9, 12, 14].

Determining the frequency of births of children with congenital anomalies is one of the most effective ways to monitor hereditary variability in human populations, and the creation of congenital anomaly registries for the purpose of monitoring hereditary variability in populations living in specific territories is necessary for planning the optimal scope of diagnostic, therapeutic, rehabilitative, and preventive measures. Monitoring developmental defects in children is a long-term system of environmental control that allows new teratogens to be identified as causes of congenital developmental anomalies through the analysis and comparison of epidemiological data [2]. Tracking the population frequency of developmental defects allows any changes to be recorded, with further investigation into the causes of the observed fluctuations [6].

Many countries around the world have created specialized registries to study the frequency and dynamics of congenital malformations. Such registries make it possible to identify the emergence of new teratogens in the environment, assess the amount of medical care required for congenital and hereditary pathologies, and evaluate the effectiveness of preventive measures, including prenatal diagnosis. Modern advances in genetics and medicine make it possible to diagnose a significant proportion of congenital malformations in a timely manner, including during the prenatal period [15, 16].

In light of the above data, it is important to study and analyze the epidemiology of congenital malformations, including determining population frequencies and assessing changes in these parameters over time.

Research objective: based on the analysis of the results of monitoring congenital malformations in the Republic of Karakalpakstan for 2020–2025, to establish the prevalence and structure and assess the dynamics of the frequency of congenital malformations.

Research methods:

A retrospective analysis of prenatal diagnosis data in the Republic of Karakalpakstan for 2020–2025 was conducted. The study included all cases of CHDs registered in medical institutions of the Republic of Karakalpakstan in 2020–2025. The source of information was official regional monitoring data. Congenital malformations were coded according to the International Classification of Diseases, 10th Revision (ICD-10).

The analysis was performed using absolute numbers and standardized EUROCAT indicators calculated per 10,000 live births. Annual indicators were used to assess dynamics, and data from 2020–2025 were used for structural analysis.

Statistical processing of the material was performed using standard statistical programs [8]. The results were presented in tables using Word version 7.0. The critical level of significance (p) was set at 0.05.

To assess the reliability of differences in VPR frequencies by year, region, and epidemiological group, the nonparametric $\chi 2$ goodness-of-fit test was used.

Research results: During the monitoring of congenital malformations (CM), all cases diagnosed for the first time in the neonatal period and during the first year of life were recorded. These malformations are classified according to Class XVII of the International Classification of Diseases, 10th Revision (‘Congenital anomalies, malformations, and chromosomal abnormalities’). The combined database thus includes information not only on mandatory registrations, but also on other congenital malformations identified during monitoring.

All regional registries took into account cases of CHD among live births and stillbirths with a body weight of more than 500 g and a gestational age of 22 weeks. However, cases of earlier fetal

death, as well as prenatally detected CHD in induced abortions, were excluded from this study. The total number of births during the study period was 228,823, of which 1,119 children with malformations were registered. To determine the frequency of malformations, data on the total number of live births in the study population was used as the denominator. The frequency of CHD was calculated per 1,000 births.

In order to assess the dynamics of the prevalence of congenital malformations (CM) in the region for the period from 2020 to 2025, an analysis of data on the number of registered cases of CM and the number of live births was carried out.

Table 1.

Frequency of all registered VPRs in the regions of the Republic of Karakalpakstan by year

Регион	2020	2021	2022	2023	2024	2025 (5 months)
Nukus	0.07	0.76	0.14	0.16	1.39	1.57
Nukus District	0.02	0.13	0.05	0.35	0.20	0.13
Tahiatash City	0.00	0.18	0.28	0.12	0.18	0.19
Khojaly District	0.01	0.46	0.92	0.78	0.51	0.94
Kegeyli District	0.01	0.25	0.26	0.16	0.35	0.31
Chimbay District	0.00	0.46	0.40	0.46	0.66	0.31
Karauyak District	0.00	0.20	0.21	0.07	0.18	0.25
Takhtakupir District	0.01	0.15	0.05	0.07	0.48	0.75
Kanlykul District	0.01	0.33	0.57	0.46	0.28	0.31
Shumanai District	0.02	0.15	0.21	0.21	0.46	0.25
Kungrad District	0.04	1.40	0.19	0.10	0.94	0.57
Muinak District	0.01	0.18	1.18	0.09	0.18	0.13
Amudara District	0.04	0.56	0.95	1.31	1.64	1.45
Beruniy District	0.10	0.10	1.40	1.48	1.57	1.76
Ellikala District	0.03	0.31	0.40	0.60	0.30	0.19
Turtkul District	0.01	0.13	0.05	0.09	0.66	1.13
Bozatau District	0.00	0.05	0.02	0.00	0.03	0.38

The results show a clear upward trend in the registered incidence of VPR. While in 2020 the rate was 0.38 per 1,000 live births, by 2025 (after 5 months) it had reached 10.18. All regions (except Boztau) saw a significant increase in the frequency of VPR in 2021 compared to 2020. During this period, the frequency increased from 0.07 to 0.76 in Nukus and from 0.04 to 1.40 in the Kungrad district.

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Nukus, Amudarya, and Berun districts show some of the highest and, as a rule, growing rates throughout the period (2022–2025). In 2024, the leaders are Berun (1.57) and Amudarya (1.64) districts.

The Kungrad district shows a high peak in 2021 (1.40) and 2022 (1.09), but then declines. The Muynak district peaks in 2022 (1.18) with low rates in other years. Low and stable rates: Nukus, Kara-Uzak, and Boz-Tau districts traditionally have lower VPR rates compared to the rest of the sample, which requires separate verification of the completeness of registration.

The sharp increase in the frequency of VPR in all regions in 2021 probably does not reflect a real epidemiological surge, but rather indicates a significant improvement in the work of the VPR registry (monitoring).

The data for 2020 (virtually zero rates in many regions) may reflect the initial stage of implementation of the monitoring system or incomplete coverage (i.e., registration was carried out carelessly or only according to a limited list of VPRs).

The observed differences in frequencies between regions (e.g., Beruniy 1.76 vs. Nukus 0.13 in 2025) require further study, as they may be caused by a combination of factors. The differences may indicate pockets of exposure to teratogenic factors (water/air pollution, industrial waste, pesticides). Given the geographical location (the Priaralye region), this may be related to an environmental disaster and its impact on public health.

Higher frequencies in urban centers (Nukus) and large districts (Amudarya, Berun) may be explained by better quality and availability of prenatal screening, more qualified personnel, and high case registration completeness. In sparsely populated areas (e.g., Bozatao), low figures may conceal the problem of underdiagnosis (insufficient detection).

Thus, the above data show that between 2020 and 2025, there will be a significant increase in the incidence of registered congenital malformations in the region. Certain areas, such as Nukus, Kungrad, Amudarya, and Berun, show the highest incidence of CHDs compared to other areas. The data obtained underscore the importance of conducting additional research to identify the etiological factors contributing to the increase in CHDs in the region.

The study also revealed the dynamics of CHD registration for the period from 2020 to 2025 (incomplete, 5 months) in the Republic of Karakalpakstan.

Table 2.

GDP dynamics in the Republic of Karakalpakstan (2020–2025)

Year	Live births	Rate per 10,000	Rate per 1,000 in ‰
2020	129	0,22	0,022‰
2021	264	3,95	0,395‰
2022	384	5,35	0,535‰
2023	361	4,90	0,490‰
2024	395	5,88	0,588‰
2025 (5 months)	169	6,64	0,664‰

Analysis of the table data showed exponential growth in the incidence of VPR, with the rate per 1,000 births increasing from 0.022‰ (2020) to 0.535‰ (2022).

After peaking in 2022, the rate declined slightly in 2023 (0.490‰), but in 2024, a steady increase to 0.588‰ was observed. The interim rate for the first five months of 2025 (0.664‰) is the highest for the entire observation period, indicating that the upward trend is continuing or intensifying.

The virtually zero registration rate in 2020 (0.022‰) and the subsequent sharp increase in 2021–2022 cannot be explained solely by a biological or epidemiological surge. This dynamic most likely reflects the process of establishing the VPR monitoring system. The 2020 figures demonstrate a critical degree of underreporting. The increase in 2021–2022 indicates a significant improvement in methodological rigor and completeness of data collection, including more active detection of cases in the neonatal period and the first year of life.

Despite improvements in registration, the current indicators for 2023–2025 remain extremely low in terms of international epidemiology. According to the recommendations of the European EUROCAT registry and other major monitoring systems, the overall burden of MR (incidence including live births, stillbirths, and medically indicated terminations) is typically 15–25 cases per 1,000 births (15–25‰). When considering only live births with BPD, the rate rarely falls below 10‰ in developed monitoring systems.

The indicators for Karakalpakstan (0.490‰ – 0.588‰) are many times lower than recognized international standards. This is a convincing scientific argument in favor of the fact that there is still a significant problem with the completeness of detection and registration of VPR in the region. Cases are most likely going unreported due to the lack of adequate prenatal screening, low rates of VPR diagnosis in newborns in remote areas, and the exclusion of medically indicated abortions from the registry.

Data for the first five months of 2025 (0.664‰), when extrapolated to the full year (assuming the registration rate remains unchanged), could potentially amount to about 1.6‰. This extrapolation confirms a steady upward trend in the registered incidence, which may be due to both a real increase in morbidity (due to environmental or other factors) and ongoing improvements in the reporting system.

Despite the low absolute figures, the steady upward trend in incidence from 2020 to 2025 requires an in-depth epidemiological investigation to distinguish between the contribution of improved registration and a possible increase in the impact of teratogenic factors in the region.

We also analyzed the structure of VPR based on monitoring data in the Republic of Karakalpakstan for 2020–2025.

Table 3

Structure of the GDP according to monitoring data in the Republic of Karakalpakstan (2020–2025)

Nosology	2020 (‰)	2021 (‰)	2022 (‰)	2023 (‰)	2024 (‰)	2025 (5 months) (‰)
Down syndrome	0,43	0,76	0,71	0,83	1,04	0,81
CHD (Congenital heart defects)	0,63	0,76	1,14	0,88	1,14	0,85
Cleft palate and lip	0,58	0,59	0,85	0,74	0,71	0,49
Reduced limb defects	0,3	0,25	0,38	0,3	0,28	0,24
Spinal cord hernia	0,3	0,23	0,14	0,14	0,15	0,24
Hydrocephalus + SMG	0,08	0,08	0,02	0	0,08	0,04
Microtia	0,18	0,28	0,26	0,12	0,33	0,12
Esophageal atresia	0,1	0,03	0,12	0,09	0,08	0
Anus atresia	0,05	0,03	0,33	0,25	0,15	0,04
Lung hypoplasia	0	0	0	0,02	0	0
Hypospadias, epispadias	0,03	0,08	0,02	0	0,05	0
Hermaphroditism	0	0,03	0	0,02	0,03	0,04
Renal agenesis, dysgenesis	0	0	0	0	0,03	0
Polydactyly	0	0,08	0,05	0,05	0,15	0,04
Congenital diaphragmatic hernia	0	0,03	0	0,02	0	0,04
Gastroschisis	0	0,03	0,05	0	0	0
Umbilical cord hernia	0	0	0	0	0,05	0
MVPR (Multiple VPR)	0,23	0,38	0,21	0,3	0,4	0,08
Others	0,35	0,38	0,38	0,37	0,4	0,33
Total frequency of VPR	**3,23**	**4,02**	**4,69**	**4,13**	**5,08**	**3,38**

Table 3 presents the total estimates of the frequencies of 18 isolated CHDs and Down syndrome for 2020–2025. Analysis of the data in the table shows that CHD (congenital heart defects) have the highest recorded frequency among all nosologies, peaking in 2022 and 2024 (1.14 ‰). There is a marked increase from 2020 to 2022, which may indicate improved diagnosis (e.g., the introduction of neonatal screening or improved ultrasound diagnosis).

The incidence of Down syndrome shows the most stable and consistent growth over the entire period, reaching 1.04 ‰ in 2024. This is probably due to the increased completeness of registration of the most obvious chromosomal abnormality.

After a noticeable increase in 2022 (0.85‰), the incidence of cleft palate and lip has stabilized, reflecting relatively complete registration of this visible defect.

The frequency of limb reduction defects remains consistently low (0.25–0.38 ‰), showing no significant upward trend.

We conducted a detailed analysis of the structure of birth defects based on monitoring data in the Republic of Karakalpakstan for 2020–2025 in comparison with data from EUROCAT (European Birth Defects Registry).

Table 4

Structure of the GDP according to monitoring data in the Republic of Karakalpakstan (2020–2025)

Nosology	Max. CR (‰)	LIVE BIRTH Prevalence (EUROCAT, ‰)
Down syndrome	1,04	≈1,0
Cleft palate and lip	0,85	≈1,0
VSD	1,14	≈3,0−6,5
Anorectal atresia	0,33	≈0,2−0,4
Spinal cord hernia	0,30 (2020)	≈0,1−0,5
Gastroschisis/Diaphragmatic hernia	<0,05	≈0,05−0,15

A comparative analysis with EUROCAT data showed that the incidence of Down syndrome fully complies with European standards for live births, indicating that this birth defect is being registered in full.

The incidence of cleft palate and lip is close to the European standard, which is expected for a visible defect. This is the benchmark for completeness of registration for obvious defects in the region.

The incidence of VSD is 3-6 times lower than expected compared to EUROCAT data, although it is the leading defect among all CHDs for 2020-2025 in the Republic of Karakalpakstan.

Anorectal atresia is within the EUROCAT range, which, as in the case of Down syndrome, confirms good registration of obvious gastrointestinal defects requiring immediate surgery.

A steady decline in the incidence of spina bifida from 0.30 ‰ (2020) to 0.14-0.15 ‰ (2022-2024), combined with low rates of hydrocephalus, may be a sign of incomplete reporting or poor prenatal screening.

Low rates (close to zero) for defects such as gastroschisis and diaphragmatic hernia, which require emergency surgery, indicate gaps in early detection.

Discussion. Analysis of monitoring data shows significant interregional variability in estimates of the overall frequency of registered congenital malformations (CM). CM frequency rates in the 17 regions studied do not reach the threshold value of 20 cases per 1,000 births. The observed range of variation in the overall CHD frequency extends from a minimum of 0.00 per 1,000 births (Bozata district) to a maximum of 1.57 per 1,000 (Nukus city).

Interpreting the identified variability is methodologically challenging due to the polyetiology of this group of pathologies, as well as the potential influence of differences in diagnostic protocols, the level of prenatal screening, and the completeness of subsequent case registration. According to EUROCAT recommendations, a VPR frequency below 20 per 1,000 births indicates incomplete detection or underdiagnosis of malformations [13]. Based on this, we assume that incomplete registration is the key factor contributing to the low overall level of registered CHDs in a number of administrative units of the Republic of Karakalpakstan.

According to EUROCAT data, congenital heart defects consistently rank first among CHDs in Europe. Our results confirm this trend: CHDs accounted for 23.5% of the total. Down syndrome and cleft lip and palate are also among the leading forms, which is consistent with international and Russian data.

The impact of the environmental situation in Karakalpakstan should be noted. A number of studies indicate an increased risk of chromosomal abnormalities and congenital defects in regions with high levels of pollution. Thus, environmental factors can be considered as one of the possible determinants of the identified characteristics.

Conclusion. The analysis of the dynamics of congenital malformations in the Republic of Karakalpakstan for 2020–2025 revealed significant fluctuations in their frequency, with the highest number of cases in 2024. The structure of CHDs was largely similar to the data from international and regional studies: congenital heart defects, Down syndrome, and cleft lip and palate consistently remain in the leading positions. These results confirm that the distribution of CHDs in Karakalpakstan corresponds to global trends, but the marked increase in rates in certain years requires a more in-depth analysis of possible causes, including improvements in diagnostics and record-keeping systems, as well as the influence of environmental and social factors.

The data obtained underscore the need for further development of the prenatal diagnosis system, increased accessibility of screening technologies, and a comprehensive approach to the prevention of congenital malformations. Strengthening monitoring and conducting additional epidemiological studies will not only clarify the true extent of the problem, but also help to develop effective measures to reduce morbidity and improve the quality of life of children in the region.

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