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MEDICAL AND ENVIRONMENTAL ASPECTS EVOLUTION OF DISEASES OF THE ENDOCRINE SYSTEM IN CHILDREN OF UKRAINE

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We have found that in 2017 9.569 cases of endocrine system diseases were detected in children affected by the Chornobyl accident (or 24,67 per 1.000 children), which is by 1.7 times higher than the mean incidence of this pathology in children in Ukraine. Methods of statistical evaluation and epidemiological analysis of state medical statistics from 1993 to 2020 were used. Throughout 25 years of observation we have discovered that from the period of 1993 to 2017 was a decrease in the incidence and prevalence of the endocrine system diseases in children by 36.9 %, and, more significantly, by 65.5 % — in children who suffered as a result of the Chernobyl accident. At the same time, disability increased by 5.3 times. The prevalence and incidence of endocrine diseases in children affected by the Chernobyl accident are significantly higher than the national mean, especially in the detection of thyroid disease.

Key words: children, morbidity, prevalence, disability, diseases of the endocrine system, Chornobyl disaster.

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МЕДИКО-ЕКОЛОГІЧНІ АСПЕКТИ ЕВОЛЮЦІЇ ХВОРОБ ЕНДОКРИННОЇ СИСТЕМИ У ЛІТЕЙ УКРАЇНИ

У дітей, які потерпіли внаслідок аварії на ЧАЕС, у 2017 році було вперше виявлено 9569 випадків хвороб ендокринної системи або 24,67 на 1000 відповідного дитячого населення, що у 1,7 разу перевищувало середній показник захворюваності на цю патологію дітей в Україні. Застосовувалися методи статистичної оцінки та епідеміологічного аналізу даних державної медичної статистики з 1993 по 2020 роки. За 25 років спостережень встановлено, що з 1993 по 2017 рік в Україні відзначалося зниження захворюваності та поширеності хвороб ендокринної системи у дітей на 36,9 %, та більш значно на 65,5 % у дітей, які потерпіли внаслідок аварії на ЧАЕС. У той же час показник інвалідності дітей унаслідок хвороб ендокринної системи у 5,3 разів перевищує аналогічні показники у 1993 році. Показники поширеності та захворюваності на хвороби ендокринної системи, розлади харчування та порушення обміну речовин дітей, які потерпіли внаслідок аварії на ЧАЕС, значно перевищують загальнодержавні показники, особливо показники виявлення захворювань щитовидної залози.

Ключові слова: діти, захворюваність, поширеність, інвалідність, хвороби ендокринної системи, Чорнобильська катастрофа.

The study is a fragment of the research project "Peculiarities of clinical progression and treatment of bronchial asthma in children with supraworld body weight and obesity", state registration No. 0120U100804.

Endocrine diseases in the modern world are a significant medical and social problem ofmankind, especially in children [8]. In parallel with the growth in the provision of the population, the increase in caloric intake and the growth in the consumption of carbohydrates and fats around the world, especially in developed countries, the incidence in the population, including children, of type 1 diabetes and obesity is growing [7, 13]. Childhood and adolescent obesity is associated with adult mortality and premature death [7]. Studies by Kostopoulou E, Güemes M, Shah P. (2020) and other scientists have confirmed the fact of special risks for children with endocrine pathology, primarily diabetes and obesity, when infected with COVID–19 [10] Of course, chronic stress, in which humanity has been in the last decades of wars and pandemics, also plays a significant role in this. This causes, particularly in children and adolescents, hyper – or hyposecretion of the stress systemmediators, which is associated with persistent neuroendocrine and epigenetic changes in the future [14].

Modern studies confirm a higher prevalence of subclinical biochemical disorders of the thyroid gland in children leading to hypothyroidism and thyroiditis, which affects the quality of children's life and their neurocognitive development [2, 9]. It should be noted that children who were observed for a long time and received therapy due to severe hypothyroidism, only in 16 % of cases had positive dynamics and recovered over time [15].

The results of scientific research have shown that there is a significant relationship between physical inactivity, poor nutrition in children, obesity, diabetes mellitus and an increased prevalence of caries and inflammatory and dystrophic diseases, including periodontal tissues and oral mucosa [4].

In addition to genetic and biological factors, negative environmental changes are extremely important for the development of endocrine pathology in children [5]. The thyroid gland in children turned out to be one of the most sensitive organs to the effects of radionuclides, especially in the context of the growth of thyroid tumors [5, 4].

Over the past decade, the prevalence and incidence of endocrine pathology among children in Ukraine has a constant annual tendency to decrease, despite the general global trend towards its growth among the child population [4]. The only objective reason for this condition is a decrease in the detection of this pathology at the primary level due to the deterioration of its diagnosis.

In view of this, constant epidemiological monitoring of the incidence and prevalence of endocrine pathology in children is essential in order to timely identify adverse trends in children's health, establish causal relationships and develop the necessary set of medical and social measures.

The purpose of the study was a retrospective analysis of trends in incidence and prevalence rates, the structure of the endocrine system diseases in children of Ukraine for the period from 1993 to 2017, including some monitoring data for 2021.

Material and methods. An assessment was made of changes in the incidence and prevalence of the endocrine system diseases, eating disorders and metabolic disorders (hereinafter referred to as ESD) in children of Ukraine, paying special attention to the child population affected by the accident at the Chornobyl nuclear power plant. Methods of statistical assessment and epidemiological analysis of state medical statistics from 1993 to 2020 were used. [14]. Statistical assessment methods were used, in particular, the Mann – Whitney signed rank U – test to compare the incidence rates of ESD in children from the same regions of Ukraine in 1993 and 2017. Cluster analysis of the ESD incidence in the children's population in the regions of Ukraine was carried out using the K – means method by correlating the incidence rates of BES in the children's population of the regions and the city of Kyiv to the level of this index in Ukraine and taking into account the presence of radiological control territories that arose as a result of the Chornobyl accident.

To determine the linear dependence and correlation, the degree of relationship between the population – weighted effective doses in milliSieverts (hereinafter referred to as mSv) of the total body exposure of residents of the country's different regions in the time period from 1997 to 2011 and the incidence of ESD in children from different regions, a calculation of Spearman's rank correlation coefficient was used [2]. The results were processed using the software product STATISTICA 6 and Excel—2010 [1].

Results of the study and their discussion. Among all registered diseases in children of Ukraine, diseases of the endocrine system, eating disorders, metabolic disorders (hereinafter referred to as BES) occupy the 4th place, and in the structure of morbidity they occupy the 11th place out of 17, which indicates their significant impact on the health status of children in Ukraine as a whole. Thus, the disability rate of children in Ukraine due to diseases of the endocrine system is now more than by 5 times higher than analogous indices in 1993. In children who suffered as a result of the Chornobyl accident, ESD in the structure of prevalence occupy a higher 3rd place, and in terms of morbidity – the 9th ranking place. This also confirms the growth during our study of the ESDprevalence proportion in the structure of all registered diseases of childhood from 2.05 % in 1993 to 3.9 % in 2017, and the incidence – from 1.0 % to 1.1 %. In general, in 2017, according to state medical statistics, the incidence of children aged 0–17 years including ESD was 110.015 newly diagnosed cases, which corresponds to 14.45 per 1 thousand of the corresponding child population (hereinafter – per 1 thousand children).

Of these, in children of the first year of life in 2017, 12.905 cases of ESD were detected for the first time, or 36.06 cases per 1,000 children. There were 50 cases of congenital hypothyroidism (0.17 per 1000 children) and 4 cases of diabetes (0.01 per 1000 children). In children affected as a result of Chornobyl disaster in 2017, were first detected 9569 cfses of endocrine system diseases or 24.67 per 1000 corresponding children's population which was by 1.7 times higher than the mean index of this pathology incidence in Ukraine. In 2021 this index had a tendency to decrease and made 21.26 per 1000 children. Also since 2010 decrease of thyroid gand's malignant tumours in children has been observed making from 0.03 to 0.02 cases per 1000 corresponding contigence. At this thyroid gland's diseases have made 64 % of the total BES incidence index in this contingence of children. Prevalence of endocrine system diseases in children affected due to Chornobyl power plant disaster in 2017 made 75413 or 194.46 cases per 1000 children which was by 2.85 times higher than the all country's index of endocrine pathology in children of Ukraine which made 68.16 cases per 1000 children or 519073 all registered cases. Morbidity in children affected due to Chornobyl power plant disaster with the thyroid gland's diseases made 16.46 per 1000 children which was by 2.64 times more than the total country's indices. The total of endocrine system

diseases in the Chornobyl contigence of children were registered in 60040 individuals or in 154.82 per 1000 children which was by 303.6 % more than the all country's indices of thyroid gland's pathology prevalence in children.

The proportion of BES prevalence in the structure of registered diseases of childhood in this contingent of children makes 8.26 %, and the incidence rate is 1.66 %, which is higher than the nationwide indices of the diseases prevalence in children and indirectly indicates the possible impact of the of the Chornobyl accident's consequences in combination with other factors on the progression of the endocrine system diseases. The above significant excess of the incidence and prevalence indices of endocrine pathology in children injured as a result of the Chornobyl accident, both in 1993 and 2017, certainly indicates the importance of radiation exposure among other factors for the occurrence of this pathology (hereditary, geochemical, etc.).

The maximum detection of endocrinological pathology was observed during monitoring in children aged 7–14 years including, which indicates the need for in – depth dispensary examinations, sanitation of chronic foci of infection (primarily dental) and the introduction of rational school meals. Over the observation period of 25 years, a moderate decrease in the specific detection of the ESD incidence in children aged 7–14 years inclusive (from 53.2 % to 49.0 % of the total number of detected cases) against the background of an increase by 1.4 times was noted in the specific dynamics of newly diagnosed cases of BES in adolescents from the total number of detected cases. In children aged 0–6 years inclusive, during the entire observation period, there was a decrease in the number of diagnosed BES by 10.1 %.

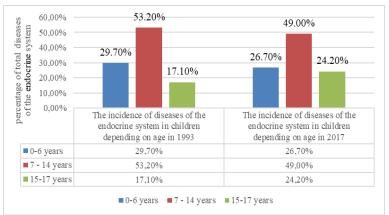


Fig. 1. Comparative characteristics of changes in the incidence of the endocrine system diseases among children depending on age (in 1993 and 2017).

Obviously, the above characterizes the period from 15 to 17 years as one of the most critical and sensitive in terms of external environmental impacts and risks. Not surprisingly, adolescents had the highest rates of prevalence and incidence of ESD–1514.2 and 246.5 per 1000 of the corresponding child population, respectively.

It should also be noted that during the monitoring period, obesity in adolescents began to be detected by 1.8 times more frequently than in 1993.

The smallest number of newly diagnosed BES cases was observed in infancy – 12905 or 36.06 cases per 1000 of the corresponding child population, which amounted to 2.41 % of all registered disease cases in children under one year of age.

Fig. 2 shows a comparison of the diseases incidence in the structure of the incidence of the endocrine system diseases in children in 1993 and 2017 in terms of the index per 1000 children. The current trend towards an increase by 1.65 times in the index of obesity incidence in children and by 2 times in the diabetes mellitus index is obvious. The incidence of thyroiditis also increased by 1.5 times. Thus, in 2017, for the first time, 20.610 cases of obesity in children were detected, which amounted to 2.71 per 1.000 children (in 1994–20.378 or 1.84 per 1.000 children) (fig. 2). The prevalence of obesity in Ukrainian children was 14.53 per 1.000 children, or 101.657 of all registered cases.

The detection of acquired hypothyroidism increased by 5 times, nodular goiter increased by 2 times and diffuse goiter of 2–3 degrees increased by 3.5 times. This may be both the result of an improvement in the diagnostic capabilities of the children's health care system, and indirect evidence of the continuing "iodine deficiency" in a number of regions of the country, as well as the lack of appropriate measures at the local level. It is also possible to have a complex effect on the children's body of negative environmental factors, especially in areas where the territories of radiological control are located after the Chornobyl accident. After all, in 1993, 7 years after the accident in Ukraine, there were already significant excesses in the incidence of thyroid diseases in children aged 0–14 inclusive, classified as victims of the Chornobyl accident. Thus, their incidence of nodular goiter exceeded the national indices by 314.3 %, diffuse goiter of the 1st degree – by 490 %, thyrotoxicosis – by 260 %, acquired hypothyroidism – by 200 %, thyroiditis – by 480 %.

It should be noted that this clearly indicates a possible negative impact of the Chornobyl accident consequences in combination with other factors on the state of the thyroid gland as one of the main targets

of radiation exposure. An alarming fact over 25 years of observation is the increase in the incidence of thyrotoxicosis in children by 1.53 times, which requires appropriate attention and study of this phenomenon. After all, one of the most common causes of hyperthyroidism can be Graves' disease (diffuse

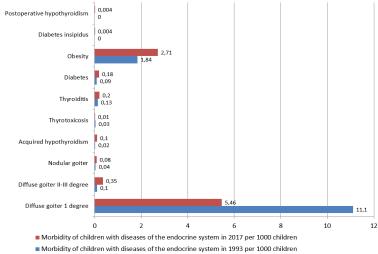
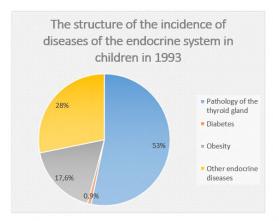


Fig. 2. Comparison of the nosologies frequency in the structure of the incidence of the endocrine system diseases in children in 1993 and 2017 in terms of per 1000 children.

toxic goiter), which requires timely diagnosis and long-term observation and treatment. At the same time, during the monitoring period, there was almost a 2 – fold decrease in the incidence of diffuse goiter of the 1st degree.

Analyzing these data, understood the difficulties that we had to face when analyzing data almost 30 vears ago, when the terms "hyperplasia of the thyroid gland of "endemic and 1st degree", sporadic goiter" appeared in the reports of medical statistics, which required their appropriate interpretation.



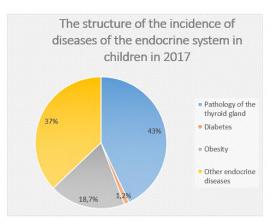


Fig. 3. Change in the representation of diabetes, obesity, thyroid diseases and other endocrine system diseases in the structure of the incidence of endocrine system diseases in children in 1993 and 2017 (in percent).

Thus, in the structure of the endocrine diseases' incidence in children in 1993, the first place certainly belonged to diseases of the thyroid gland, which accounted for 43.0 %. These include: diffuse goiter grade 1–3, nodular goiter (endemic and non – toxic), thyroiditis, acquired and postoperative hypothyroidism, thyrotoxicosis. Obesity (17.6 %) was in the 2nd place, and other diseases of the endocrine system (28.0 %), which were not included in official medical statistics, were in the 3rd place. Diabetes mellitus (0.9 %) took the 4th place. During the observation period, this structure, as it can be seen from fig. 3, has been preserved, but has undergone certain changes: there was a tendency to a moderate increase in the proportion of obesity (up to 18.7 %) and diabetes mellitus (up to 1.2 %), as well as other endocrine diseases. (37 %), which reflects the dynamic increase in the incidence of these diseases. At the same time, the proportion of thyroid diseases decreased by 10 % and reached 43 %, primarily due to a decrease in the incidence rate of diffuse goiter of the 1st degree.

It should be noted that during the 25 years of observation in Ternopil, ,Luhansk, Khmelnytsky, Mykolaiv and Zhytomyr and Zaporizhzhya, Kherson regions and Kyiv, there was a significant increase in the incidence of children with BES, more than by 2 times. While in Chernivtsi, Dnipropetrivsk, Kherson, Odessa and Vinnitsa regions, there was a decrease in similar indices.

As it can be seen from fig. 4, the incidence rate of BES in the children's population of Ukraine has decreased by 36.9 % over 25 years. In children who suffered as a result of the Chernobyl accident, it decreased more significantly – by 65.5 %. The incidence of thyroid diseases in Ukrainian children also decreased by 55.4 % in the course of observation, and in children who suffered as a result of the Chornobyl accident, it decreased even more significantly – by 71.24 %. Obviously, this reflects a faster rate of decrease in the incidence of ESD in them due to the fact that over time, the intensity of the influence of the effects

that cause these pathological conditions has changed. In 2017, the incidence rate of ESD in this cohort of children exceeded the national index by 70.73 %, and the prevalence of ESD among them exceeded the national index by 2.8 times (p<0.01). Throughout the entire observation period, the incidence rates of the endocrine system and thyroid gland diseases in children who suffered as a result of the Chornobyl accident significantly exceeded similar nationwide incidence and prevalence rates. Obviously, this reflects the delayed effects of the Chornobyl accident's consequences on the body of children born from persons who suffered from the Chornobyl accident, and their descendants in the second and third generations. In 1993, the incidence rate of ESD in children who suffered as a result of the Chornobyl accident also exceeded the national figure by 212 %, and the prevalence rate was even higher – by 225.0 %, which reflected the degree of damage to the endocrine organs, primarily the thyroid gland, in children who were evacuated in 1986 from the city of Pripyat and the exclusion zone and were directly exposed to the radiation factor, as well as children who permanently at that time lived in the zones of unconditional and guaranteed resettlement.

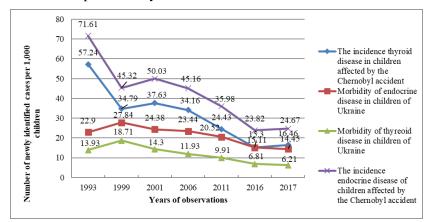


Fig. 4. Comparative dynamics of the incidence rates of children in Ukraine with the endocrine system and thyroid gland diseases per 1000 of the corresponding child population and similar indices of children affected by the Chernobyl accident (1993–2017).

The incidence rate of children affected by the Chornobyl accident with thyroid diseases in 1993 also exceeded the national index even more significantly - by 310.9 %. In this regard, we should once again return to the problem of iodine deficiency in the regions affected by the Chornobyl accident (Ukrainian Polissya is one of the most iodine - deficient regions of Ukraine). Obviously, combination of pathological factors could be the basis for the

occurrence and maintenance of a high incidence in thyroid pathology. Despite the absence of iodine isotopes in the environment at the present stage, long – term low – intensity radiation of long – lived strontium, cesium, and plutonium isotopes continues, which supports the destabilization of cell membranes and causes the development of a number of pathological processes, including those of the endocrine system [2, 11].

That is why during our monitoring, against the background of the general trend of reducing the incidence and prevalence of ESD in Ukrainian children, the expected convergence with the national values of these indices in children who suffered as a result of the Chornobyl accident did not occur (table 1).

Table 1
Indices of children's disability due to endocrine system diseases from 1993 to 2021
(According to the Center for Medical Statistics of the Ministry of Health of Ukraine)

N	Name of the index	Absolute number of children with disabilities at the end of the reporting year		Figure 1 for 10.000 children		Density		Absolute number of children with disability diagnosed for the first time in the reporting year		Figure for		Growth rate of index 1 (in %) from 1993 to 2021
		1993	2021	1993	2021	1993	2021	1993	2021	1993	2021	
1.	Total	121818	162214	92.98	217.5	100.0	100.0	19029	13149	14.5	17.5	+133.2 %
2.	Diseases of the endocrine system	4756	17106	3.6	22.9	4.0	10.5	1025	2093	0.78	2.8	+536.1 %

Diseases of the endocrine system are among the most common in the child population of Ukraine, which, of course, determines a significant number of children who have developed disabilities due to this pathology in the dynamics of our monitoring. As it can be seen from the data presented in table 1, in 2021, 17.106 children with disabilities due to ESD were registered in Ukraine, which amounted to 22.9 cases per 10.000 children. For the first time, disability was established for 2093 children with ESD, which corresponds to 2.8 cases per 10.000 children. In the structure of diseases that led to disability, short stature and hypothyroidism, diabetes mellitus with complications and neoplasms of the thyroid gland dominated [3].

Compared to 1993, the number of children who were diagnosed with disability for the first time increased by 15.3 %. In 1993, the disability rate due to ESD was 3.86 per 1.000 children, which is by 5.3 times lower than the disability rate in 2021. The specific disability in children due to ESD, among other causes, increased from 4.0 % to 10.5 % over 25 years of observation, which is obviously a consequence of an increase in the severity of endocrine pathology and its complications in children. According to the results of the performed correlation analysis, it was found that the Spearman correlation coefficient (p) was 0.568, and the relationship between the incidence and prevalence of the endocrine system diseases in children aged 0-14 inclusive in 2011 and the population – weighted effective dose (in mSv) total whole body exposure of residents of different regions in Ukraine for the period 1997–2011. was considerable and statistically significant (p<0.01) [15]. The highest levels of morbidity in children with ESD were observed in Rivne, Ivano - Frankivsk and regions, which were characterized by the presence of territories of radiological control after the Chornobyl disaster. Among other regions, Ternopil and Transcarpathian regions were the clear leaders in the incidence of children with BES [11]. Among the first ten leading regions in terms of the prevalence of endocrine pathology in Ukraine, seven have areas of radiological control after the Chornobyl accident. The maximum prevalence of diabetes mellitus was observed in children from the most developed industrial regions: Kharkiv, Lugansk, Donetsk, Vinnytsia, Lviv, Kyiv regions and in Kyiv. The low incidence rates of BES children from Chernihiv, Kharkiv, Poltava, Zaporizhzhya, Odesa and Donetsk regions can be explained by their low detection rate, due to the insufficient work of the primary health care link to identify this pathology and the shortage of medical personnel. So, even in Kyiv, the coverage of medical examinations of children with BES in recent years did not exceed 75 % [5].

Conclusion

The rates of prevalence and morbidity of the endocrine system diseases, eating disorders and metabolic disorders in children who suffered as a result of the Chornobyl accident significantly exceed the national indices, especially the rates of detection of thyroid diseases. During the 25–year monitoring in children of Ukraine, there has been a trend towards an increase in the frequency of detection of obesity, hypothyroidism, nodular goiter, thyroiditis and diabetes mellitus, especially in school – age children and adolescents, against the background of a general decrease in the incidence and prevalence of endocrine pathology and an increase in disability, which requires training of personnel, development of state programs, appropriate treatment and preventive measures.

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