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EPIDEMIOLOGY, PROGNOSIS AND RISK FACTORS FOR DEVELOPMENT OF ONCOLOGICAL DISEASES AS EARLY DIAGNOSTIC OF DENTAL PROBLEMS IN THE CHILDREN

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ABSTRACT

Introduction. In the world trends in incidence and death rates for all cancers combined and for the leading cancer types by sex, racial/ethnic group, and age were estimated by analysis and characterized by the average annual percent change during recent 5 years. Aim of research: to determine epidemiology of oncological diseases in the children population of rural clusters due to the chemical contamination of drinking water sources. Materials and methods. Analysis of water-related health indicators in the children population. Drinking water quality monitoring included studies of chemical and salt composition of water from centralized (38260 studies) and decentralized (24586 studies) water supply systems carried out in rural clusters of Dnipropetrovsk region. Results. As a result of discriminant analysis, a plausible model probable development of cancer among children population in rural clusters of Dnipropetrovsk region, which consumed drinking water from decentralized drinking water sources was obtained. Conclusions. According to the correlation analysis was determined that oncological morbidity among children population responded quickly to the changes in salt and chemical composition of water from centralized and decentralized drinking water systems. In 3, 4, 5, 6 clusters of Dnipropetrovsk region high levels of morbidity this class of diseases (*r=0,763, p=0,077*) were observed in children who consume wells water with high nitrate content (at the limit of MPC 45 mg / dm^3). It was established that prognostic capacity for a model of development cancer in children under 14 years is 34%. During 2014–2019 years tendency of negative growth of tumors in the children population of Dnipropetrovsk region in all clusters was established: 1 (-20.9 %), 2 (-37.5 %), 3 (-31.1 %), 4 (-33.8 %), 5 (-22.3 %), 6 (-29.2 %).

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Introduction. In the world trends in incidence and death rates for all cancers combined and for the leading cancer types by sex, racial/ethnic group, and age were estimated by analysis and characterized by the average annual percent change during the most recent 5 years (2012-2016 for incidence and 2013-2017 for mortality) [1]. Among children younger than 15 years, cancer incidence rates increased an average of 0.8% per year during 2012 to 2016, and cancer death rates decreased an average of 1.4% per year during 2013 to 2017 [2]. Among adolescents and young adults aged 15 to 39 years, cancer incidence rates increased an average of 0.9% per year during 2012 to 2016, and

cancer death rates decreased an average of 1.0% per year during 2013 to 2017 [3]. Data on cancer deaths were obtained from the National Center for Health Statistics National Vital Statistics System. Stage distribution and 5-year survival by stage at diagnosis were calculated for breast cancer, colon and rectum (colorectal) cancer, lung and bronchus cancer, and melanoma of the skin [4]. Among children, overall cancer incidence rates increased by 0.8% per year from 2010 to 2014, and overall cancer death rates decreased by 1.5% per year from 2011 to 2015 [5].

Leukemia is a malignant disease of the hematopoietic organs resulting from progressive cell hyperplasia in the hematopoietic organs, when processes of cell division (proliferation) prevail over the processes of maturation (differentiation) [6]. Pathological substrate of the disease is leukemic blast cells that correspond to the parental elements one of the hematopoietic germs. There are acute and chronic leukemia. On the basis of clinical, morphological and cytological picture, separate variants of acute leukemia are distinguished: myeloblastic, lymphoblastic, monoblastic, promyelocytic, undifferentiated. Criterion for differentiating forms of the disease is the cytochemical characteristic of pathomorphological substrate. *Acute leukemia* occurs mainly at a young age. In most cases, disease develops gradually, its harbingers appear long before an acute attack. General weakness, easy fatigue, pain in the muscles, joints, bones, throat, an increase in the submandibular and cervical lymph nodes, subfebrile temperature are noted. Symptoms of the advanced phase of untreated acute leukemia are diverse and cover all the most important systems of the body [7]. Clinical picture of acute leukemia is determined by 4 leading syndromes: hemorrhagic, hyperplastic, anemic and intoxication. Basis of the hemorrhagic syndrome, which is detected in 50-60% of patients, is a sharp thrombocytopenia, which develops as a result of suppression of normal hematopoiesis by hyperplasia and bone marrow infiltration. Hemorrhagic syndrome manifests itself in the form of petechiae, ecchymosis, hematomas on the skin and oral mucosa, or profuse bleeding [8].

In the oral cavity, the most typical characteristic is a sharp bleeding of the gums, presence of hemorrhages on the mucous membrane on the cheeks along line of closing the teeth, on the tongue, palate [9]. Sometimes significant hemorrhages and hematomas are found. Such changes are combined with non-specific manifestations in the form of decreased appetite, weakness, fatigue, and increased body temperature [10]. In the dental practice, manifestations of hemorrhagic syndrome can be mistaken accepted for a consequence of biting mucous membrane (with single hemorrhages, especially along the line of closing teeth on the mucous membrane on the cheeks), for manifestation of hypovitaminosis C, which leads not only to incorrect diagnosis, but also to unreasonable interventions. Confirmation of the diagnosis is a blood test or bone marrow aspirate [11].

Hyperplastic processes are manifested by an increase in lymph nodes in 50% of patients, liver, spleen, tonsils - in 25%. Gingival hyperplasia is detected in 5% of patients, as usually in a severe course of the process, and regarded by hematologists as unfavorable prognostic sign. Hyperplasia and infiltration of the gums by leukemic cells are peculiar. Sometimes it is so significant that crowns of the tooth are almost completely covered with a loose, bleeding shaft. Often, hyperplasia is combined with necrotic ulcerative changes in the gums. In addition, necrosis is also found on the tonsils, in the retromolar region and other parts of the oral mucosa. Feature of the necrotic process in acute leukemia is its tendency to spread to neighboring areas, as a result of which unlimited ulcers of irregular contours appear, covered with a gray necrotic plaque. Reactive changes around the ulcer are absent or mild [12].

In the patients with acute leukemia, taste sensitivity is impaired — taste perception a part of mushroom papillae is lost. The appearance of pain in intact teeth and jaws, along with pain in other bones, which arise as a result of direct damage to the bones in the leukemic process, was noted. In the patients with leukemia, on the background of a sharp decrease the body's resistance, candidiasis often develops [13]. According to a number of authors, fungal lesions of oral mucosa arise as a result of specific leukemic process and action of antibiotics, cytostatics, corticosteroids. Task of the dentist is the early diagnosis disease of the blood system by dental and other manifestations, blood analysis. Treatment of underlying disease is carried out in a special hematological or therapeutic department [14].

Aim of research: to determine epidemiology of oncological diseases in the children population of rural clusters due to the chemical contamination of drinking water sources.

Materials and methods of research. Analysis indicators of population health and main aspects of the deterioration health status in the children population related to environmental factors, first of all, pollution of drinking water systems. Ecological and hygienic monitoring of drinking water quality included study of the chemical and salt composition of water samples, taken from centralized

(38260 studies) and decentralized (24586 studies) sources of water supply in 6 clusters of Dnipropetrovsk region for 2014-2019 years.

By the following levels of resources development, such as socio-economic and urban development and analysis of the dendrogram towards clustering administrative districts of Dnipropetrovsk region, the following groups of clusters were identified (Fig. 1).

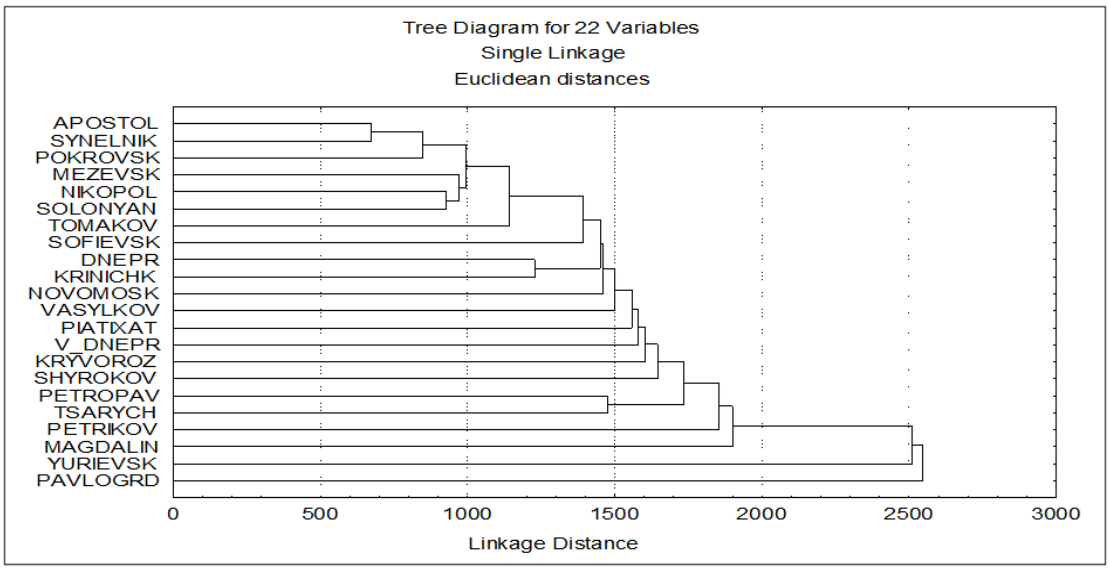

Fig. 1. Dendrogram of clustering administrative districts of Dnipropetrovsk region by the level of socio-economic and urban development.

Cluster 1 – covers Kryvorizhsky and Novomoskovsky rural districts of Dnipropetrovsk region. This cluster is characterized by a high indicator of resource potential and high levels of socio-economic and urban development.

Cluster 2 – Nikopolsky and Pavlogradsky districts characterized by average level of resource potential and high level of socio-economic and urban development.

Cluster 3 is Dnipropetrovsk district. This cluster is characterized by high level of potential and average level of socio-economic and urban development.

Cluster 4 includes Vasylkivsky, Krynichansky and Sinelnikovsky districts of Dnipropetrovsk region, which have average level of resource potential and average level of socio-economic and urban development.

Cluster 5 covers Verkhnodniprovsky, Mezhivskyi, Petrykivskyi, Pyatikhatskyi, Sofiyivskyi and Shyrokivskyi districts. This cluster is characterized by a low potential and average level of socio-economic and urban development.

Apostolovsky, Magdalenivsky, Petropavlovsky, Pokrovsky, Solonyansky, Tomakivsky, Tsarichansky and Yurevsky districts form *cluster 6*. This is the largest cluster of rural population. It is characterized by the lowest indicator of resource potential and low level of socio-economic and urban development.

In the individual clusters a correlation was established between the chemical and salt composition of drinking water and incidence and prevalence of cancer among children population. The relationship between quantitative variables was determined by pairwise Pearson correlation coefficient. Multidimensional statistics, such as discriminant analysis and cluster analysis were used as auxiliary mathematical methods in the separate stages of study. Horizontal dendrograms were used for cluster analysis. For the discriminant analysis, a classification function, posterior probabilities, and a summary matrix were used to estimate specific sensitivity and overall predictive reliability. *Excel* was used for the initial preparation of tables and intermediate calculations. Most of the mathematical processing was performed on PC using standard statistical package *STATISTICA 10.0 portable.*

Results of research and discussion. Incidence of oncological diseases among children from 0 to 14 years was probably highest by long-term indicators in the cluster 1: 19.92±1.81 ‰ ($p<0.05$) and cluster 5: 19.59±3.04 ‰ ($p<0.001$). In this case, this class of diseases exceeded average regional incidence rate (16.92±0.48 ‰) in 1.78 times (1 cluster) and in 1.02 times (5 cluster), with positive growth rates in the regions: from + 17.7 to +15.8%. In general, incidence rate II class of diseases in the

children population never exceeded average regional level (25.20±0.39) ‰ in all clusters of Dnipropetrovsk region (*p<0.001*).

During 2014–2019 years, tendency of negative growth oncological diseases in the Dnipropetrovsk region was established in all rural clusters: 1(-20.9%), 2(-37.5%), 3 (-31.1%), 4 (-33.8%), 5 (-22.3%), 6 (-29.2%). Extensive rate of tumors among children in some clusters of the region is varied: from 0.09% (in 3 cluster) to 0.21% (in 4 cluster) (Fig. 2).

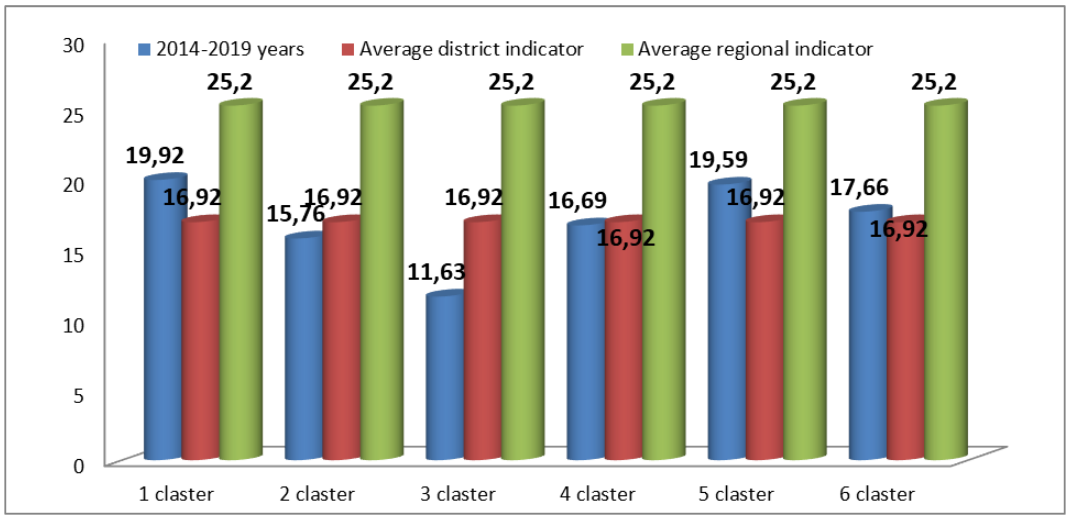

Fig. 2. Incidence of oncological diseases in children population up to 14 years in the clusters of Dnipropetrovsk region (cases per 10,000 of children).

Dynamics prevalence of oncological diseases during 2014-2019 years is characterized by probable decreasing its rates in all clusters of Dnipropetrovsk region: from (43.09 ± 5.38) to (39.30 ± 3.16) cases per 10,000 children *(p<0.05).* However, the highest prevalence II class of disease is observed in 3 cluster: (69.40±3.42) ‰ (*p<0.001*) with positive growth rates in rural districts (+62.1%) and in the region (+16.5%). It was shown exceeding average district indicator for the prevalence of this class of diseases in 1.62 times, and average regional indicator – in 1.16 times.

The lowest incidence of neoplasms is probably determined among children under 14 years in the 2nd cluster: (29.35±3.47) ‰ (*p<0.001*) with negative growth rates by districts (31.4%) and by the region (-50.7%) (Fig. 3).

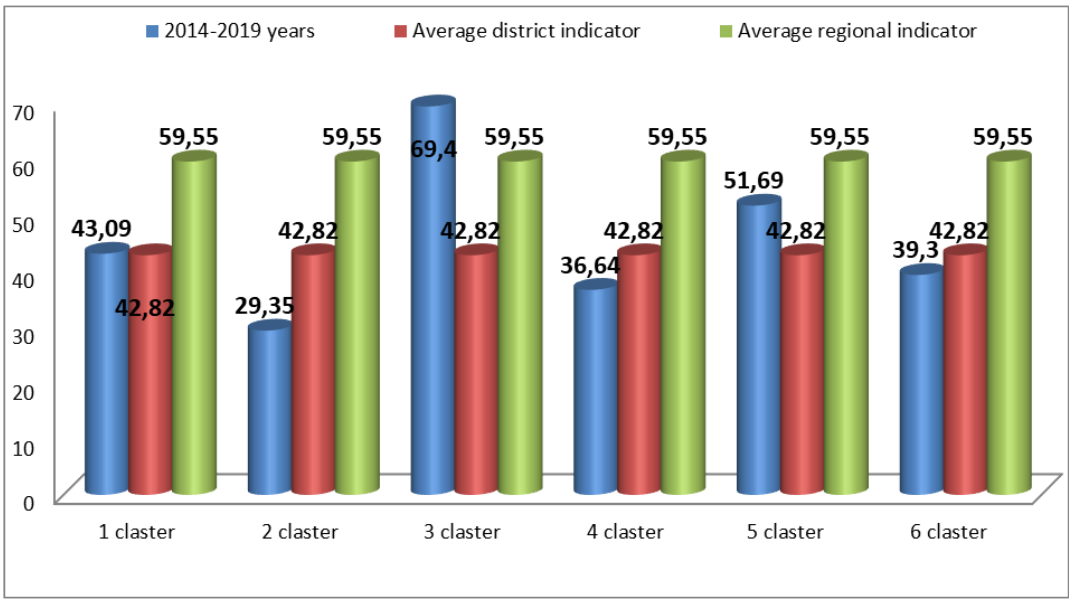

Fig. 3. Prevalence of oncological diseases in children population up to 14 years in the clusters of Dnipropetrovsk region (cases per 10,000 of children).

As a result of discriminant analysis a plausible model probable development of oncological diseases was obtained in children population living in rural clusters of Dnipropetrovsk region, which

consumed drinking water from decentralized drinking water sources. The model investigated likelihood of developing a prevalence of cancer in children aged from 0 to 14 years by some indicators of drinking water quality taken from decentralized water systems, which appeared to be the most informative and influence on the discrimination (*F=3.93; p<0.001*). As a result, the following classification functions are obtained:

$Cancer_0 = -199.52 + 0.02Dz_{\text{dry residue}} + 163.42\ Dz_{Cu} + 5.75\ Dz_{Al} - 0.097\ Dz_{Mg} + 0.086\ Dz_{Cl^-} + 3683.03\ Dz_{Mn} - 0.73\ Dz_{\text{rigidity}}$,

$Cancer_1 = -191.52 + 0.02\ Dz_{\text{dry residue}} + 141.14\ Dz_{Cu} + 14.49\ Dz_{Al} - 0.08\ Dz_{Mg} + 0.083\ Dz_{Cl^-} + 3610.58\ Dz_{Mn} - 0.70\ Dz_{\text{rigidity}}$.

where: $Cancer_0$– function of absence probability of developing oncological diseases among children; $Cancer_1$ – function of presence probability of developing oncological diseases among children; Dz – indicators of drinking water quality in decentralized water supply systems: Dz_{rigidity} – by general rigidity; $Dz_{\text{dry residue}}$ – by dry residue; Dz_{Cu} – by copper content; Dz_{Al} – aluminum; Dz_{Mn} – manganese; Dz_{Cl^-} – chlorides; Dz_{Mg} – magnesium. Thus, for children population of rural areas in Dnipropetrovsk region, specificity of this classification is 11%, sensitivity is 23%, which indicates reliability of general prognostic ability towards development of cancer – 34%.

According to the correlation analysis it was shown that incidence and prevalence of oncological diseases at the children living in 2 claster correlated with a high content of nitrates in water of centralized systems with underground water sources (*r=0.646, p=0.023; r=0.504, p=0.095*).

In the territory of 3, 4, 5, 6 clusters of Dnipropetrovsk region was observed high levels of morbidity on cancer in children (*r=0.763, p=0.077*) which corresponds to the high levels of nitrates in water, because nitrates have a carcinogenic effect. In the 3rd cluster, indicators of organic water pollution in decentralized systems were mostly influenced on the development of oncological pathology among children population. In particular, ammonia nitrogen affected on increasing incidence of cancer (*r=0.813, p=0.049*).

Conclusions.

1. According to the correlation analysis was determined that oncological diseases among children population were quickly reacted on the changes of salt and chemical composition of water from centralized and decentralized drinking water systems. In particular, in 3, 4, 5, 6 clasters of Dnipropetrovsk region high levels of morbidity this class of diseases in children (*r=0.763, p=0.077*) observed with consumption of underground drinking water with high nitrate content (on the limit of MPC 45 mg/dm^3).

2. It is established that general prognostic capacity a model of development oncological diseases among children under 14 years is 34 %. In particular, probability of development chronic diseases of circulatory system caused excess of salts (general rigidity and dry residue), copper, aluminum, manganese, chlorides, magnesium in water from decentralized rural water supply systems (*F=3.93; p<0.001*).

3. During 2014–2019 years tendency of negative growth of neoplasms among children population living in Dnipropetrovsk region was established in all clusters: 1 (-20.9 %), 2 (-37.5 %), 3 (-31.1 %), 4 (-33.8 %), 5 (-22.3 %), 6 (-29.2 %). Extensive rate of neoplasm in children from some clasters ranges from 0.09 % (in cluster 3) to 0.21 % (in cluster 4).

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