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ЭПИДЕМИОЛОГИЯ АУТОИММУННОГО ТИРЕОИДИТА У ДЕТЕЙ АРКТИЧЕСКОГО РЕГИОНА НА ПРИМЕРЕ АРХАНГЕЛЬСКОЙ ОБЛАСТИ В 2014–2023 ГГ.

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РЕЗЮМЕ. ***Введение.*** Аутоиммунный тиреоидит является актуальной проблемой детской эндокринологии в связи с его негативным влиянием на рост и развитие ребенка. В Арктическом регионе, к которому относится часть Архангельской области, по сравнению с южнее расположенными районами России, предрасположенность к аутоиммунным заболеваниям реализуется в более раннем возрасте. С учетом изменяющихся климатических условий, пандемии новой коронавирусной инфекции, а также изменения экологической ситуации актуальна оценка заболеваемости аутоиммунным тиреоидитом у детей Архангельской области за длительный период времени с целью обоснования целесообразности поиска ранних маркеров начала аутоиммунной тиреопатии и поиска рычагов воздействия на аутоиммунный процесс. ***Цель.*** Проанализировать динамику распространенности и первичной заболеваемости аутоиммунным тиреоидитом у детского населения Архангельской области за период 2014–2023 годов. ***Методы.*** В данной работе проведена оценка общей и первичной заболеваемости аутоиммунным тиреоидитом у детей: 1) по данным статистических форм № 12 «Сведения о числе заболеваний, зарегистрированных у пациентов, проживающих в районе обслуживания медицинской организации», 2) по данным учетных форм 025-1/у по обращаемости в областные и городские медицинские учреждения Архангельской области за период 2014–2023 годов. ***Результаты.*** Выявлен рост распространенности аутоиммунного тиреоидита в Архангельской области за последнее десятилетие. Первичная заболеваемость остается на прежнем уровне. Распространенность аутоиммунного тиреоидита гетерогенна и зависит от района. В части Арктических регионов (город Северодвинск, Архангельск, Новодвинск, а также Приморский район) выше, чем в других регионах Архангельской области. Лидирующие позиции по частоте распространенности аутоиммунного тиреоидита занимает г. Северодвинск. ***Выводы.*** Возникает необходимость в более глубоком, комплексном обследовании детей с данной патологией, особенно проживающих в Арктическом регионе, с целью ранней диагностики и профилактики прогрессирования аутоиммунного тиреоидита, а также запуска мультиорганного аутоиммунного синдрома.

КЛЮЧЕВЫЕ СЛОВА: *щитовидная железа, аутоиммунный тиреоидит, заболеваемость, арктический регион, дети*

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EPIDEMIOLOGY OF AUTOIMMUNE THYROIDITIS IN CHILDREN OF THE ARCTIC REGION EXEMPLIFIED BY THE ARKHANGELSK REGION IN 2014–2023

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ABSTRACT. ***Introduction.*** Autoimmune thyroiditis is a pressing issue in pediatric endocrinology due to its negative impact on the growth and development of the child. In the Arctic region, which includes part of the Arkhangelsk region, compared with the southern regions of Russia, a predisposition to autoimmune diseases is realized at an earlier age. Taking into account changing climatic conditions, the pandemic of a new coronavirus infection, as well as changes in the environmental situation, it is important to assess the incidence of autoimmune thyroiditis in children in the Arkhangelsk region over a long period of time in order to justify the feasibility of searching for early markers of the onset of autoimmune thyroidopathy and finding levers of influence on the autoimmune process. ***Objective.*** To analyze the dynamics of prevalence and primary incidence of autoimmune thyroiditis in the child population of the Arkhangelsk region for the period 2014–2023. ***Methods.*** In this work we assessed the overall and primary incidence of autoimmune thyroiditis in children: 1) according to statistical forms No. 12 "Information on the number of diseases registered in patients living in the service area of a medical organization"; 2) according to registration forms 025-1/u on visits to regional and city medical institutions of the Arkhangelsk region for the period 2014–2023. ***Results.*** The prevalence of autoimmune thyroiditis has increased in the Arkhangelsk region over the past decade. Primary morbidity has generally remained at the same level. The prevalence of autoimmune thyroiditis is heterogeneous and depends on the region, and in some Arctic regions (the city of Severodvinsk, Arkhangelsk, Novodvinsk, and the Primorsky district) it is higher than in other regions of the Arkhangelsk region. The city of Severodvinsk holds a leading position in the prevalence of autoimmune thyroiditis. ***Conclusions.*** There is a need for a more in-depth, comprehensive examination of children with this pathology living in the Arctic region, for the purpose of early diagnosis and prevention of the progression of autoimmune thyroiditis, as well as the onset of multiorgan autoimmune syndrome.

KEYWORDS: *thyroid gland, autoimmune thyroiditis, morbidity, Arctic region, children*

INTRODUCTION

Autoimmune thyroiditis (AIT) is one of the most common autoimmune diseases and the main cause of acquired primary hypothyroidism in children [1]. The prevalence of AIT in the world is heterogeneous and varies widely.

According to the literature, the prevalence of AIT among the adult population varies depending on the region and socio-economic level and ranges from 4.8 to 25.8% in women and 0.9–7.9% in men [2].

According to a systematic review and meta-analysis by Xiaojie Hu, Yuquan Chen, the overall prevalence of AIT in adults was 7.5%, with 17.5% in women and 6.0% in men. The risk of developing AIT in adult women is approximately 4 times higher than in adult men [3]. According to W.M. Tunbridge et al., in the United States, 10% of the population have antibodies to the thyroid gland, the prevalence is 14% in whites and about 5% in blacks [4].

The frequency of clinically overt forms of AIT among the population of the Republic of Belarus reaches 1% [5], while subclinical hypothyroidism and elevated levels of antithyroid antibodies in the blood can be detected in 10–15% of practically healthy people [6].

In the Russian Federation, AIT affects 3–4% of the population. Asymptomatic carriage of antibodies to thyroid peroxidase in the general population reaches 30% [7].

According to E.A. Troshina et al., over a 10-year period (2009–2018), a statistically significant increase in the incidence of thyroiditis in the Russian Federation is noted. The median incidence over 10 years was 44.8 cases per 100,000 people. This may be due to the growth of autoimmune pathology, improved diagnostics, and, in some cases, overdiagnosis [8].

The prevalence of AIT in children is less studied. According to A.V. Kiyaev, the prevalence of AIT among children and adolescents is 1.4% [9].

Over the past decade, there have been no large analytical epidemiological studies in the literature on thyroiditis, in particular AIT, in the pediatric population. There is very little data on the incidence of antibody carriage and subclinical hypothyroidism.

The Arkhangelsk region (AR) is the largest subject of the Russian Federation in the north of the European part of Russia. It belongs to the regions of the Far North and equivalent to them, and part of the AR, namely: municipalities — the city of Arkhangelsk, the city of Severodvinsk, the city of Novodvinsk, districts — Mezensky, Leshukonsky, Onezhsky, Pinezhsky and Novaya Zemlya — to the Arctic regions. Moreover, the urban agglomeration — Arkhangelsk, Severodvinsk, Novodvinsk — has large city-forming industrial enterprises.

According to available scientific data, for children of the AR, along with desynchronosis in the process of formation of the immune system in early ontogenesis, signs of a decrease in the reserve capacity of the immune defense and an increase in autoimmunity are characteristic. Due to the influence of a complex of unfavorable factors (climatic, geographical and technogenic) in the conditions of the Arctic region, a predisposition to autoimmunity is realized earlier [10].

In the "THYRCOV" study, which included 287 patients with COVID-19, hypothyroidism was detected in 5.2%, and thyrotoxicosis in 20.2% [11]. Subacute thyroiditis is often a consequence of COVID-19 [12–14].

It is assumed that SARS-CoV-2 can also act as a trigger for autoimmune thyroid disease. SARS-CoV-2 infection plays a role in triggering or enhancing autoimmune diseases among susceptible patients, or worsening pre-existing autoimmune disorders, which increases the likelihood of developing autoimmune thyroiditis, as well as autoimmune polyglandular syndromes in these patients [11]. Given changing climatic conditions, the pandemic of a new coronavirus infection, as well as changes in the environmental situation, it is necessary to assess the incidence of AIT in children in the Arkhangelsk region over a long period of time in order to justify the feasibility of searching for early markers of the onset of autoimmune thyroidopathy and finding levers of influence on the autoimmune process.

MATERIALS AND METHODS

This work assesses the incidence of autoimmune thyroiditis in children:

1) according to statistical forms No. 12 "Information on the number of diseases registered in patients living in the service area of a medical organization" under the ICD-10 code "E 06" for the period 2014–2023;
2) according to registration forms 025-1/u — on visits to regional and city medical institutions of the Arkhangelsk region (State Budgetary Healthcare Institution of the Arkhangelsk Region "Arkhangelsk Regional Children's Clinical Hospital named after P.G. Vyzhetsov", city children's medical institutions of large cities (Arkhangelsk, Severodvinsk, Novodvinsk, Kotlas, Koryazhma, Velsk)) for the period 2014–2023.

The indicators of general incidence (prevalence) and primary incidence of thyroiditis, in particular autoimmune thyroiditis, were studied.

In order to assess the demographic characteristics of the population of the Arkhangelsk region, the annual reports of the State Statistics Committee on natural population movement and migration processes were studied. A statistical analysis of the incidence of autoimmune thyroiditis in children was carried out, taking into account demographic, climatic, economic and technogenic factors.

Subsequently, the dynamics of these parameters were assessed using statistical methods. To assess the dynamics of prevalence and incidence, linear regression models were built, the regression slope (coefficient b) was calculated. Using Student's t-test, an assessment of the statistical significance of the difference in the coefficient from zero was made. The presence of dynamics was considered statistically significant at $p < 0.05$.

Data processing was carried out using Microsoft Excel 2019.

RESEARCH RESULTS AND THEIR DISCUSSION

During the processing of statistical form No. 12 for the ICD-10 code (E 06) "Thyroiditis", a statistically significant increase in the overall incidence (prevalence) among children in the Arkhangelsk region was revealed in dynamics over the past 10 years from 126.94 to 238.4 per 100 thousand children (b=6.78 at p=0.028, R^2=0.47) (Fig. 1). This may be due to a decrease in the child population of the AO from 212,694 in 2014 to 193,785 in 2023.

The average prevalence of AIT over the past 10 years is 179 per 100 thousand children, from 0.12

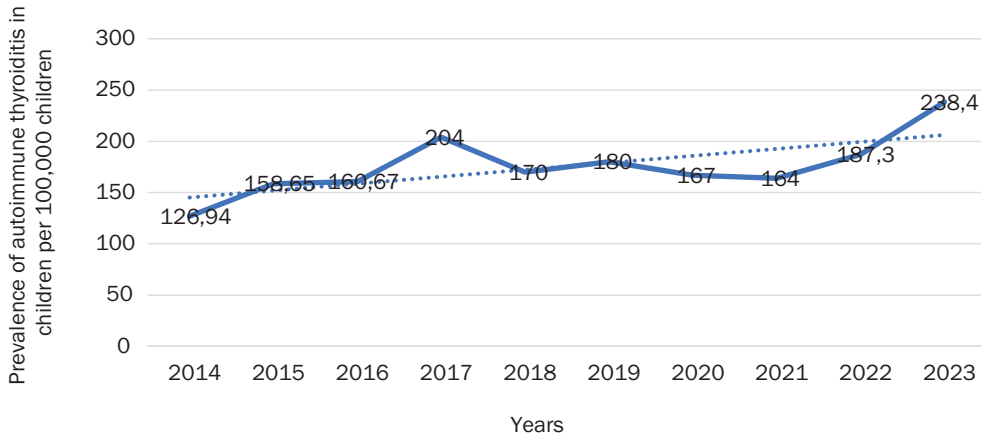

Fig. 1. Dynamics of the prevalence of autoimmune thyroiditis in children of the Arkhangelsk region per 100,000 child population for the period 2014–2023

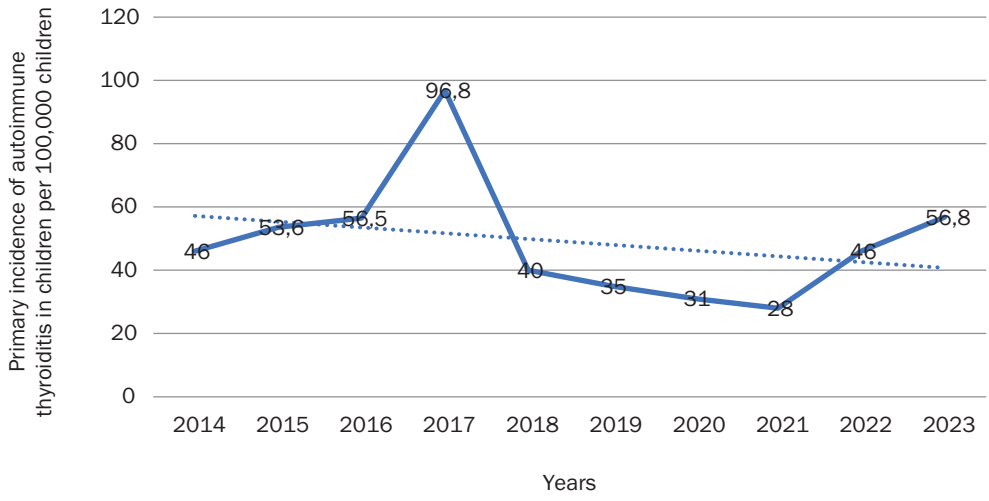

Fig. 2. Dynamics of primary incidence of autoimmune thyroiditis in children of the Arkhangelsk region per 100,000 child population for the period 2014–2023

to 0.2%, which corresponds to Russian indicators (0.1–1.2%). Thus, according to E.N. Sibileva, the prevalence of AIT in children by visits in 2003 was 32.9 per 100 thousand children. Thus, over the past 20 years, a sevenfold increase in the prevalence of AIT in children in the Arkhangelsk region has been noted.

In the Arkhangelsk region, the primary incidence of thyroiditis over 10 years averages 49 per 100,000 children. At the same time, no statistically significant changes in this indicator were found (b=–1.82 at p=0.432, R^2=0.078). However, a peak in the growth of primary incidence was noted in 2017 (Fig. 2). The decrease in prevalence and primary incidence in the period from 2019 to 2022 requires reflection and may be associated with a decrease in detection against the background of a shortage of specialists (pediatric endocrinologists).

According to E.V. Ogryzko et al., the overall incidence of thyroiditis among children aged 0–17 years in the Russian Federation in 2018 was 134.6 per 100,000 of the child population, of which 81.5 per 100,000 of the population at the age of 0–14 years, and 464.1 per 100,000 of the child population at the age of 15–17 years. The primary incidence of thyroiditis among children aged 0–17 years in the Russian Federation in 2018 was 31.3 per 100,000 of the child population, of which 20.9 per 100,000 of the population at the age of 0–14 years, and 95.6 per 100,000 of the population at the age of 15–17 years [15]. Thus, in 2018, the prevalence (in the Arkhangelsk region — 177.9 versus 134.6 per 100,000 children in the Russian Federation) and primary incidence (in the Arkhangelsk region — 57 versus 31.3 per 100,000 children in the Russian Federation) of thyroiditis in the Arkhangelsk region are higher than in Russia as a whole.

An analysis of the incidence of AIT in children living in the city and in rural areas was conducted. The share of the urban child population suffering from AIT ranges from 83.4 to 93.7% of the total number of patients in the Arkhangelsk region.

We analyzed the incidence of the urban child population using the example of the five largest cities of the Arkhangelsk region. These include: 1) Arkhangelsk industrial agglomeration: Arkhangelsk (home to enterprises of the timber processing industry, fishing and fish processing industries, mechanical engineering and ship repair), Severodvinsk (called the center of nuclear shipbuilding in Russia), city-forming enterprises — PA Sevmash, ship repair center Zvyozdochka, PA Arktika), Novodvinsk (Arkhangelsk Pulp and Paper Mill); 2) Kotlas (the main industries are mechanical engineering and metalworking, forestry and woodworking); 3) Koryazhma (an enterprise of the timber industry complex of OJSC Ilim Group); 4) Novodvinsk (JSC Arkhangelsk Pulp and Paper Mill).

The city of Severodvinsk occupies a leading position in the prevalence of AIT (Fig. 3). A statistically significant increase in the prevalence of AIT among children in Severodvinsk over the past 10 years was revealed, from 192 to 359 per 100,000 children (b=21.4 at p=0.000154, R^2=0.848) (Fig. 4). Currently, the prevalence of AIT in Severodvinsk exceeds the prevalence in Arkhangelsk by 1.5 times. An increase in the primary incidence of AIT in Severodvinsk was noted from 60.4 to 175 per 100,000 children (b=4.88 at p=0.32, R^2=0.122) from 60.4 to 176.2 per 100,000 children

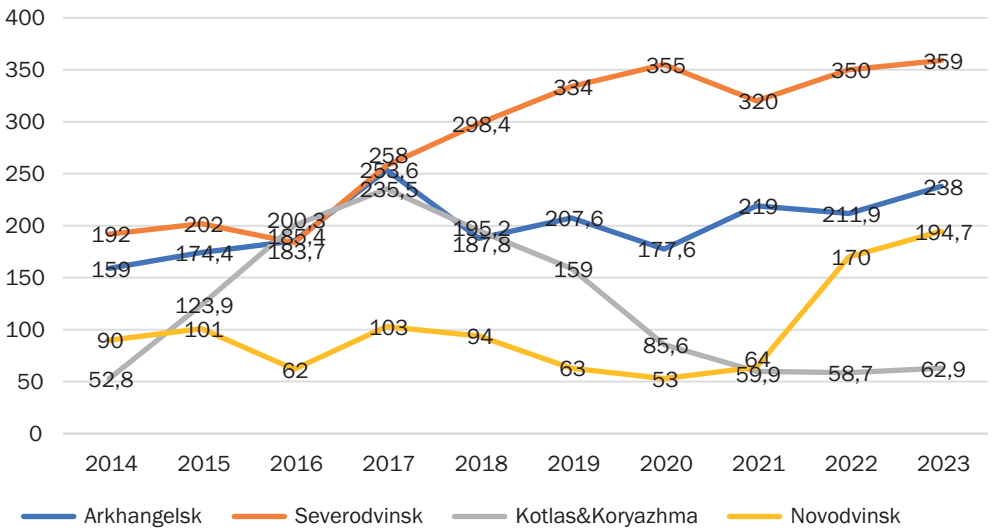

Fig. 3. Dynamics of the prevalence of AIT in children in five large cities of the Arkhangelsk region per 100 thousand children for the period 2014–2023

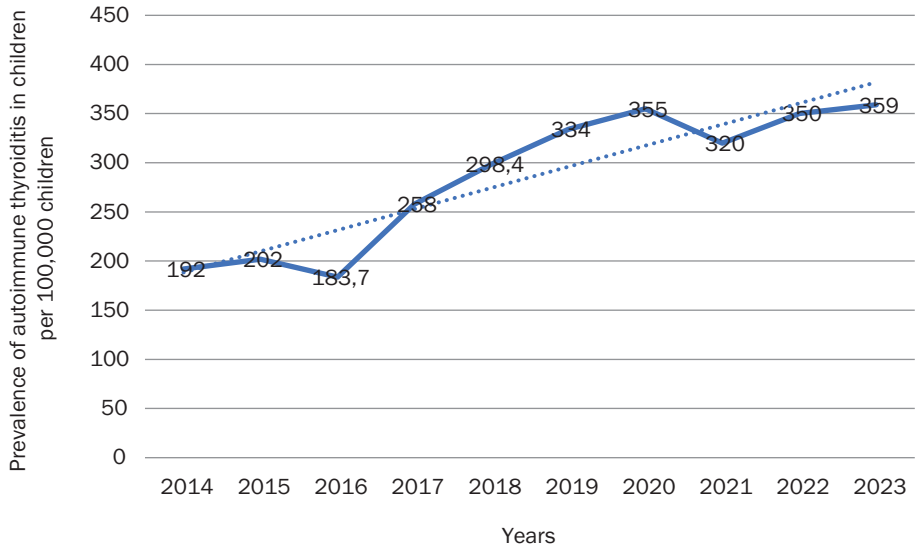

Fig. 4. Dynamics of the prevalence of AIT in children in Severodvinsk per 100,000 children for the period 2014–2023

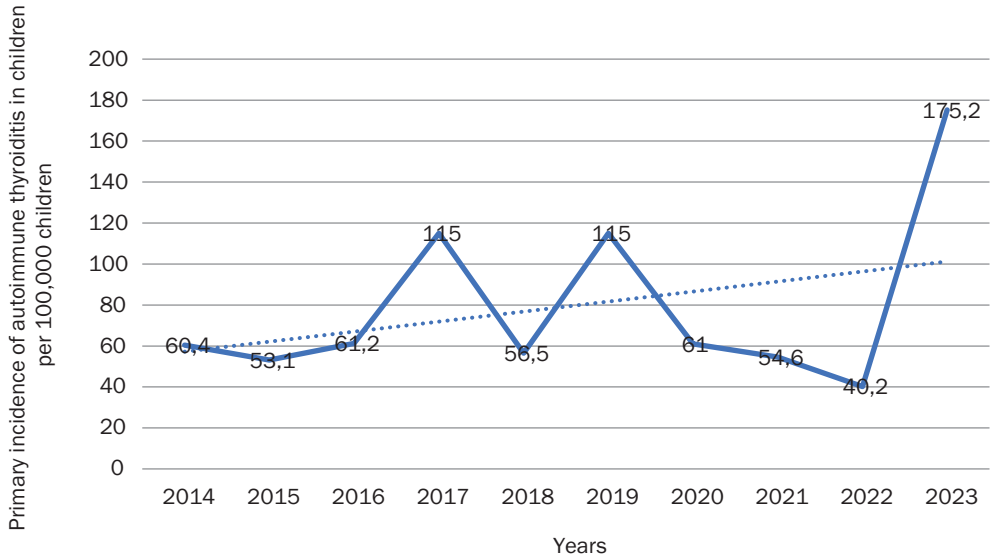

Fig. 5. Dynamics of primary incidence of autoimmune thyroiditis in children of Severodvinsk per 100,000 children for the period 2014–2023

(Fig. 5). A longer observation period is required to obtain statistically significant data.

There was a statistically insignificant increase in the prevalence of AIT among children in Arkhangelsk over the past 10 years from 159 to 238 per 100,000 children (b=5.56 at p=0.1, R^2=0.297). The primary incidence of AIT among children in Arkhangelsk in total over the past 10 years remains at the same level (b=–4.3 at p=0.188, R^2=0.2), despite the fact that there is a significant decrease in the gross emission of pollutants into the atmosphere. According to L.F. Popova et al., gross emissions of pollutants (sulfur dioxide, carbon monoxide, nitrogen oxide, hydrocarbons, volatile organic compounds) decreased by 71.8% over 10 years since 2010 (due to the fact that the Arkhangelsk Thermal Power Plant switched to burning natural gas instead of fuel oil, and the Solombala Pulp and Paper Mill was shut down in December), while the volumes of pollutant emissions into the atmosphere from motor vehicles did not change significantly in 2014–2018 [16].

The continued high level of primary morbidity may be due to a complex deterioration in overall health. According to a number of authors, the number of children with health group 1 in various regions of Russia ranges from 8 to 36%, with group 2 — from 46.5 to 57% [17]. An increase in the prevalence of AIT in Novodvinsk has

been noted over the past 2 years to 194.7 per 100 thousand children. In 2003, according to E.N. Sibileva, the prevalence of AIT in Novodvinsk was 90.8 per 100 thousand [10]. Thus, over the past 21 years, a twofold increase in the prevalence of AIT in Novodvinsk has been revealed. According to the report of the Ministry of Natural Resources and Forestry Complex of the Arkhangelsk region, among the child population of the Arkhangelsk region, the highest levels of endocrine system pathology are noted in Krasnoborsky district (64.5‰), Ustyansky District (62.9‰) and in Severodvinsk (48.4‰). In terms of morbidity among adolescents, the areas with the highest risk are Severodvinsk (201.7‰), Konoshsky district (128.6‰), and Kotlas (84.1 ‰).

We present data on the incidence of AIT in children living in rural regions of the AO (Fig. 6). Of the 21 districts of the AO, at present (as of 01.01.2024), the highest prevalence of AIT is observed in Vinogradovsky district (second only to 3 large cities of the AO) — 204.3 per 100,000 children, then in Primorsky district — 146.3, in Kholmogorsky district — 144.3, Pinezhsky district — 131.5, Krasnoborsky district — 120.5 per 100,000 children.

The prevalence of AIT varies widely, which may be due to a lack of micronutrient intake, vitamin D, and the environmental situation in the regions.

There was a statistically insignificant increase in the prevalence of AIT among children in Arkhangelsk over the past 10 years from 159 to 238 per 100,000 children (b=5.56 at p=0.1, R^2=0.297). The primary incidence of AIT among children in Arkhangelsk has remained at the same level over the past 10 years (b=–4.3 at p=0.188, R^2=0.2), despite the fact that there has been a significant decrease in gross emissions of pollutants into the atmosphere. According to L.F. Popova et al., gross emissions of pollutants (sulfur dioxide, carbon monoxide, nitrogen oxide, hydrocarbons, volatile organic compounds) decreased by 71.8% in 10 years from 2010 (due to the fact that the Arkhangelsk CHPP switched to burning natural gas instead of fuel oil, the work of the Solombalsky Pulp and Paper mill has been stopped since December), whereas the volume of emissions of pollutants into the atmosphere from motor vehicles did not change significantly in 2014–2018 [16]. Maintaining a high level of primary morbidity may be associated with a complex deterioration in general health. According to a number of authors, the number of children with the 1st health group in various regions of Russia ranges from 8 to 36%, from the 2nd — from 46.5 to 57% [17]. There has been an increase in the prevalence of AIT in Novodvinsk over the past 2 years to 194.7 per 100 thousand children. In 2003, according to E.N. Sibileva, the prevalence of AIT in Novodvinsk was 90.8 per 100 thousand [10]. Thus, over the past 21 years, a twofold increase in the prevalence of AIT in Novodvinsk has been revealed. According to the report of the Ministry of Natural Resources and the Timber Industry of the Arkhangelsk region, among the children of the Arkhangelsk region, the highest incidence of endocrine pathology is observed in Krasnoborsky district (64.5%), Ustyansky district (62.9%) and in Severodvinsk (48.4%). According to the incidence of adolescents, the territories of maximum risk are Severodvinsk (201.7%), Konoshsky district (128.6%), Kotlas (84.1%). We present data on the incidence of AIT in children living in rural regions of the AO (Fig. 6). Of the 21 districts of the AO, currently (as of 01.01.2024) the highest prevalence of AIT is observed in the Vinogradovsky district (second only to 3 large cities of the AO) — 204.3 per 100,000 children, then in the Primorsky district — 146.3, in Kholmogorsky district — 144.3, Pinezhsky district — 131.5, Krasnoborsky

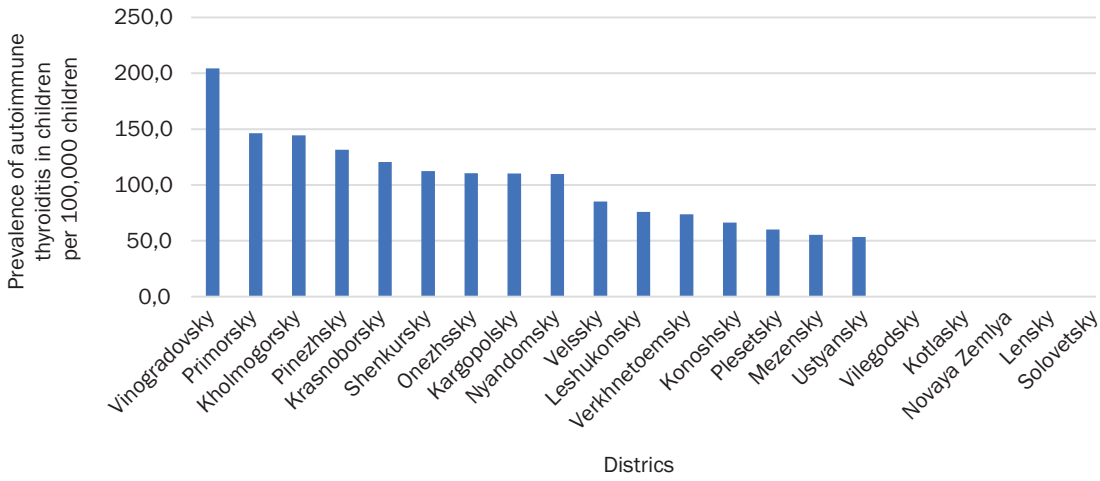

Fig. 6. Prevalence of AIT in children of Arkhangelsk region by districts per 100 thousand children for the period 2014–2023

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district — 120.5 per 100,000 children. The prevalence of AIT varies widely, which may be due to a lack of consumption of trace elements, vitamin D, as well as the environmental situation in the regions.

CONCLUSIONS

1. The prevalence and primary incidence of thyroiditis among children in the Arkhangelsk region is generally comparable to the all-Russian indicators.

Moreover, in dynamics since 2014, a statistically significant increase in the prevalence of AIT in the Arkhangelsk region was revealed with a peak in 2017. The prevalence of AIT in some Arctic regions (Severodvinsk, Arkhangelsk, Novodvinsk, and Primorsky District) is higher than in other regions of the Arkhangelsk region.

2. Despite the improvement of the environmental situation in the region, due to the complex deterioration of general health, the primary incidence remains at the same level.

A longer observation period is required to identify statistically significant dynamics in primary incidence.

3. Traditionally, the share of the urban child population suffering from AIT ranges from 83.4 to 93.7% of the total number of patients in the Arkhangelsk region. The city of Severodvinsk occupies a leading position in the prevalence of AIT, where a statistically significant increase in prevalence has been identified over the past decade.

Taking into account the increasing prevalence and morbidity, it is necessary to identify AIT at the early stages of development, including by examining children at risk (diabetes mellitus, Down syndrome, celiac disease), as well as the introduction of an early care and prevention system.

There is a need for a deeper comprehensive examination of children with this pathology, the search and introduction of new pathogenetic treatment methods.

It is also necessary to screen for other autoimmune diseases associated with autoimmune thyroiditis, especially in regions with a high incidence of AIT.

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов. Все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед публикацией.

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.

Информированное согласие на публикацию. Авторы получили письменное согласие законных представителей пациентов на публикацию медицинских данных.

ADDITIONAL INFORMATION

Author contribution. Thereby, all authors made a substantial contribution to the conception of the study, acquisition, analysis, interpretation of data for the work, drafting and revising the article, final approval of the version to be published and agree to be accountable for all aspects of the study.

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