The Influence of Regional Geological and Geochemical Factors on the Incidence of Type 1 Diabetes Mellitus

A. Zlobina, L. Farkhutdinova, I. Farkhutdinov, A. Farkhutdinov

***Abstract*—This study is aimed at identifying patterns of distribution of type 1 diabetes mellitus (T1D) incidence in the Republic of Bashkortostan (Russia), taking into account the geological and geochemical features of the territory. The influence of carbonate and granite-gneiss rocks on the distribution of diabetes incidence in the republic was noted, which may be due to the peculiarities of the chemical composition of these rocks. There is an association between increased concentration of uranium in the drinking water scale and the hair of T1D patients in some districts with the unfavourable situation of T1D. The study of uranium content in hair of T1D patients revealed its increase by 1.7 times compared to healthy individuals.**

***Keywords*—Environmental health, Geoecology, Medical Geology, Uranium, Calcium, T1D.**

I. Introduction

Type 1 diabetes mellitus (T1D) is one of the most pressing medical and social problems. Today, the number of patients in the world is about 10 million, and the incidence of the disease has been increasing annually by 3% over the past decades. The disease manifests mainly in childhood and adolescence, requires lifelong insulin therapy, and is characterized by the development of severe complications.

Currently, the development of T1D is associated with the action of environmental factors that cause autoimmune destruction of insulin-producing cells against the background of genetic predisposition, but the information on external factors and mechanisms of their influence is extremely insufficient. Recent studies have shown that the target of the immune system attack in T1D is the protein coat of the gene, which allowed to call T1D an environmental disease. The importance of the living environment is evidenced by a significant variation of epidemiologic indicators of T1D in different geographical areas. Thus, the maximum incidence (more than 20 cases per 100,000 children per year) is registered in Northern Europe and Sardinia, and the minimum (3 per 100,000) – in Venezuela, Peru, Mexico, South Korea and China [1]–[3]. In addition, the role of the external environment is indicated by data on the increased incidence of T1D among migrants [4].

One of the possible external factors is the regional geo-ecological conditions, the influence of which is determined by the specific geochemical environment of the place of residence. Analysis of the patterns of T1D prevalence from the point of view of geoecology has revealed a connection with zones of uranium-bearing granites, which are widely represented on the Scandinavian peninsula and the island of Sardinia. A number of studies show the influence of trace elements distributed in rock, water, soil on the development of the disease, but such works are few, and their results are often contradictory.

It should be emphasized that the Republic of Bashkortostan represents a unique opportunity to study the biological role of geo-environmental conditions, since its territory has a wide range of well-studied geological settings.

The aim of this study was to investigate the role of geological and geochemical factors in the development of T1D on the example of the Republic of Bashkortostan.

II. Materials and Methods

A. Study region

The study was conducted in the Republic of Bashkortostan (RB) – a region of central Russia. Geologically, the western part of the RB is represented by a vast plain confined to the southeastern margin of the East European Platform, and the eastern part – to the mountains of the Southern Urals. A wide range of geological structures (platform, foothill trough, folded area) and rocks (sedimentary, volcanogenic, igneous, metamorphic rocks of different composition, structure and age) determines the specificity of the microelement composition of the area and allows assessing the biological role of geological and geochemical factors.

B. Sampling and analyses

Hair sampling was performed in accordance with the IAEA recommendations. Hair samples were taken from people with type 1 diabetes mellitus and a control group (relatively healthy people). Age, sex, full name, address, and place of birth were recorded when samples were taken.

In total, 37 samples from the study group and 10 samples

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from the control group were analyzed.

The concentration of calcium and uranium in the hair of children was studied using instrumental neutron activation analysis using the research nuclear reactor IRT-T TPU. The contents of chemical elements were determined by comparing the radiation intensity of samples and reference samples in selected gamma photopeaks. The relative standard error in element determination was 5-15%.

C. *Public health data*

Data on the incidence of type 1 diabetes mellitus for 2017-2021 were obtained from the Medical Information and Analytical Center of the Republic of Bashkortostan (Ufa, Russia).

D. *Data processing*

For data processing, the Statistica 10 and Microsoft Excel 2013 software packages were used. A map was built using the ArcGIS 10.2.

III. Results

A. *Spatial distribution of T1D incidence in the Republic of Bashkortostan*

Mapping of the incidence rate of T1D revealed a significant variation on the territory of the Republic of Bashkortostan – from 0.27 to 2.38, the average value is 1.24 (Fig. 1).

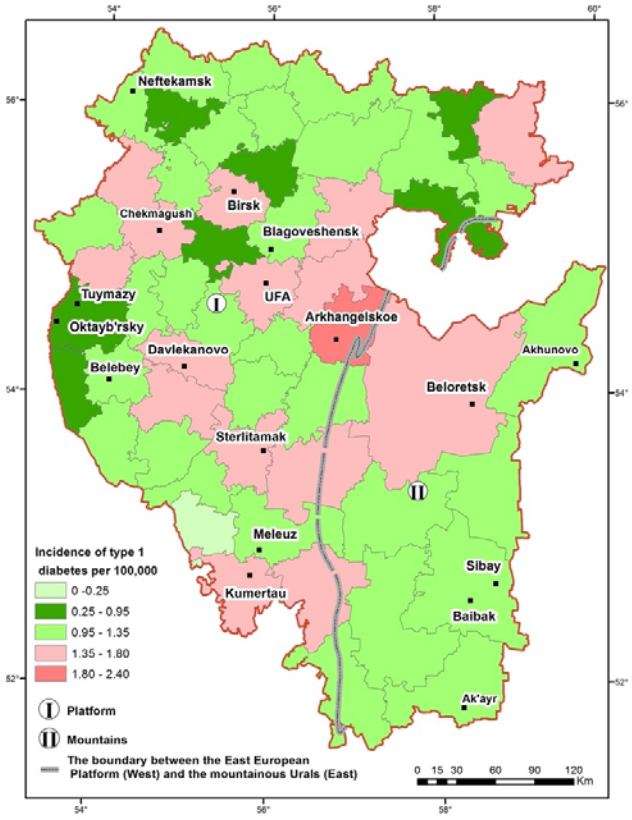

Fig. 1. Spatial distribution of T1D incidence in the Republic of Bashkortostan.

At the same time, the analysis of the disease prevalence in terms of geological conditions of the living environment revealed certain regularities. The most extensive zone with a low level of T1D incidence rate (0.59–1.54) was found in the northen part of the platform and is confined to the most extensive area of Palaeozoic carbonate rocks. Attention is drawn to the comparative uniformity of T1D abundance indicators in this zone, which also agrees with the peculiarities of element-impurity distribution in the areas of limestones. The latter are of marine origin and, therefore, are characterized by a relatively uniform distribution of trace elements over the area. At the same time, the platform part of the RB, except for the north-east, is predominantly composed of sediments of fluvial genesis, which are characterized by a mosaic pattern of element-impurity content due to the nature of their accumulation. The accumulation of trace elements takes place in relief depressions, where the water flow velocity decreases. This pattern corresponds to a rather varied prevalence of T1D in the platform part of RB.

It should be noted that the limited zone with minimal incidence of T1D on the western edge of the platform part of RB (Tuimazinsky and Yermekeevsky districts, 0.85 and 1.11) coincides with localized areas of limestones outcrops.

The favorable influence of carbonate rocks on the risk of T1D development, apparently, is caused by the peculiarities of elemental composition, in which the main share belongs to calcium – up to 95%.

Calcium is not synthesized in the body, coming mainly from food like all minerals. However, minerals compete for the absorption system, so calcium is the most important regulator of the intake of other microelements into the body and prevents the excessive accumulation of those chemical elements that can cause negative effects even at low concentrations [5,6]. The effect of calcium on carbohydrate metabolism is due to its participation in the exocytosis of insulin from the beta cell and activation of enzymes regulating glucose metabolism [7]. Thus, the available data on the physicochemical features of carbonate rocks, the influence of microelements contained in them on carbohydrate metabolism, and the role of calcium in maintaining the microelements status of the human body confirm the probable protective value of carbonate rocks in the development of T1D.

The analysis of T1D distribution in the mountainous part of the republic revealed predominantly low rates of T1D affection, which may also be related to the influence of geological conditions. Thus, the wings of the Bashkir meganticlinorium contain Paleozoic carbonate strata, in which river channels are predominantly located, including the Belaya River, the largest water artery of the republic.

At the same time, the northern district of the mountainous part, confined to the Bashkir meganticlinorium, is characterized by a relatively high prevalence of T1D (1.62). This zone is composed of Precambrian Riphean-Vendian (Mezo-Neoproterozoic) strata of enormous thickness exceeding 10,000 m. These sediments are poor in trace elements, as they represent a destruction products of granite-gneiss crystalline basement of the East European Platform. Unlike ultrabasic and basic rocks, granite-gneisses

contain a higher amount of silicic acid and belong to sialic (Si+Al) rocks.

It is noteworthy that a group of districts adjacent to the high-mountainous part of the Bashkir anticlinorium from the west (eastern districts of the platform: Nurimanovsky, Iglinsky, Arkhangelsky) are characterized by a relatively high incidence of T1D, including maximum value (Arkhangelsky, 2.38). The destruction products of granite-gneiss rocks can be the nourishment of rivers for the territory of the listed districts, witch located hypsometrically lower. The river streams that originate in the northwestern part of the Bashkir meganticlinorium flow here. The same factor, apparently, has an importance in the relatively unfavorable situation on T1D on the northeastern edge of the republic (Belokataisky district, 1.34). Near the eastern border of this area granite-gneiss rocks of the northern part of the Bashkir meganticlinorium come to the day surface (Taratash Mountain). Water arteries flowing through the northeastern region of Bashkortostan originate there.

The association of a higher risk of T1D with zones of granite-gneiss deposits is consistent with the literature data on the high prevalence of T1D in countries where these rocks are widespread, as discussed earlier. It can be assumed that the negative impact of granites is caused by depletion of essential microelements and increased content of uranium. Worldwide averages of uranium in granites are 3.9 mg/kg, however there are high radioactive granites with > 25 mg/kg of uranium [8]. On the one hand, the biological role of uranium is unknown, on the other hand, it is found in all tissues of the human body. There is information about the ability of uranium to displace calcium from bone tissue, which suggests its similar effect on the beta-cells of the pancreas [9].

B. Uranium characteristic in drinking water

Uranium enters the human body mainly through drinking water. In previous studies, we showed the spatial distribution of uranium in the scale of drinking water in RB [10]–[11]. The distribution of uranium across the territory demonstrates the connection between its concentration in drinking waters and the incidence of T1D: the zone with a relatively low uranium content (northen part of the platform) are geographically confined to districts of a low value of T1D incidence, while in the zone with higher uranium content (western and southern parts of the platform) the majority of districts with a high prevalence of T1D are located. At the same time, certain more local zones do not correspond to this pattern (the mountainous part), which is apparently due to the more complex nature of the relationship, which is influenced by other factors. Nevertheless, in general, a negative effect of uranium in the natural environment on the development of T1D can be traced.

Clinical manifestation of T1D is preceded by a long period (several years), during which antibodies to pancreatic tissues are detected, which apparently reflects the presence of a factor provoking autoimmunization. In this regard, attention should be paid to the fact that radioactive elements in low doses activate the immune system, and with increasing dose or exposure duration induce autoimmune processes with cell destruction. It should be taken into account that the absorption of radioactive elements by children's organism is more intensive than in adults due to a higher rate of metabolic processes.

C. Statistical parameters of calcium and uranium content in hair

Our previous studies have shown that the U content in the hair of children with a high degree of reliability (Pearson correlation coefficient r=0.895, reliability of approximation R^2=0.801) depends on its concentration in drinking water scale [7]-[8]. The results of correlation analysis reflect the intensity of uranium intake into the human body with drinking water. Uneven spatial distribution of trace elements in drinking water and hair of healthy children depending on geological and geo-ecological conditions on the territory of RB was also noted [10].

Statistical parameters of Ca and U content in hair of study group (patients with T1D) and control group are presented in the Table 1. The statistical analysis showed that the average concentrations of calcium in hair in the study group (0.265 mg/kg) are insignificantly lower than in the control group (0.294 mg/kg). Uranium has a different trend, in the study group its content in hair (0.056 mg/kg) is 1.7 higher than in the control group (0.033 mg/kg).

TABLE I: STATISTICAL PARAMETERS OF CA AND U CONTENT IN HAIR OF THE RESIDENTS OF THE REPUBLIC OF BASHKORTOSTAN

Statistical parameters	Ca in hair of study group, mg/kg (N=37)	Ca in hair of control group, mg/kg (N=10)	U in hair of study group, mg/kg (N=37)	U in hair of control group, mg/kg (N=10)
Arithmetic mean	0.265	0.294	0.056	0.033
±Standard error	±0.044	±0.057	±0.010	±0.009
Median	0.270	0.325	0.061	0.029
Minimum	0.010	0.040	0.001	0.001
Maximum	1.325	0.546	0.296	0.098
Standard deviation	0.265	0.182	0.061	0.030
Skewness	1.941	-0.040	2.174	1.147

This result confirms the assumption about the provocative role of uranium in the development of carbohydrate metabolism disorders.

Moreover, we noted the uneven distribution of uranium in the hair of T1D patients across the platform and mountainous areas (Fig. 2). Increased average uranium concentration were marked in western districts of the platform, which is consistent with the unfavourable situation of T1D in some districts (Chekmagushevsky and Sharansky).

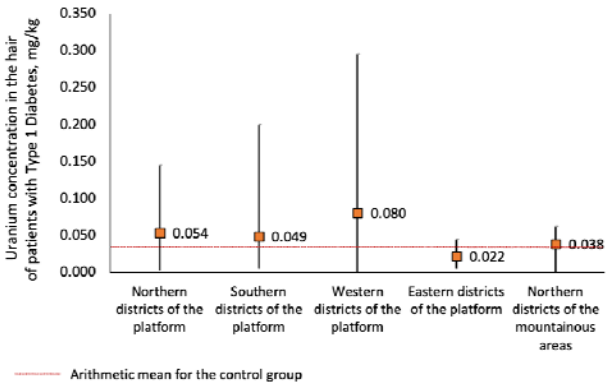

Fig. 2. Uranium concentration in the hair of T1D patients in the Republic of Bashkortostan

The data available in the literature about uranium accumulation in the pancreas and spleen allow us to think about the possibility of its activating effect on the immune system with an increase in the formation of antibodies to the pancreatic tissue and the development of autoimmune processes underlying the pathogenesis of T1D. Clarification of the role of uranium in the development of T1D and elucidation of the mechanisms of its negative impact on carbohydrate metabolism require further more detailed study.

IV. Conclusions

Analysis of the prevalence of T1D in in the Republic of Bashkortostan revealed regularities reflecting the relationship with regional geological and geochemical conditions. A decrease in the prevalence of the disease was found in the zones of carbonates, which suggests their protective role. The favorable influence of limestones and dolomites, apparently, is caused by the peculiarities of their chemical composition, in which the ratio of calcium and other impurity elements is close to their interrelation in the human body. The positive value of calcium is probably connected with its participation in regulation of carbohydrate metabolism and ability to prevent accumulation in the body of microelement provoking its disorders. According to the results of the conducted research, the zones of higher level of T1D prevalence are territorially confined to the areas of granite-gneiss rocks occurrence, which are characterized by depletion of vital and enrichment of radioactive microelements, first of all uranium. The study of uranium distribution on the territory of RB revealed an increase in the incidence of T1D in areas of higher uranium content in drinking water and human hair. The study of uranium content in hair of T1D patients revealed its increase by 1.7 times compared to healthy individuals. There is an association between uranium increased concentration in the drinking water scale and the hair of T1D patients in some districts with the unfavourable situation of T1D. These facts consistent with the hypothesis about the provoking effect of uranium on the development of carbohydrate metabolism disorders and indicates the need for further research in this direction.

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