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Iodine and selenium in natural waters as a risk factor in manifestation of endemic thyroid diseases (review)

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Iodine is an essential microelement for the production of thyroid hormones that regulate the normal development and functioning of living organisms. Therefore, this element is the most important factor responsible for endemic thyroid disease because both insufficient and excessive iodine intake can cause thyroid disorders. In addition, according to numerous researches, the occurrence of thyroid pathologies may also be related to deficiency of other trace elements, such as selenium which is also involved in the metabolism of thyroid hormones. Despite the fact that according to usual diet estimates intake of iodine with water does not exceed 5–10% of its total uptake, both water and water contained in fresh food are better digested and have a higher physiological value. Therefore iodine and selenium content in drinking water are worth to be considered in relation to endemic thyroid pathology. The paper presents a review of publications devoted to investigation of iodine and selenium content in natural waters as a possible factor contributing to development of thyroid malfunctions and endemic goiter among local residents. Analysis of the published data shows that iodine concentration in water can be used in assessment of the iodine status of the territories in context of the element deficiency or excess as a health risk. Relationship between low iodine concentration in drinking water and manifestation of endemic goiter among the local population is most pronounced in the regions characterized by its combination with low water selenium and iodine deficiency in soils. The disease may also be provoked by high iodine in drinking water. Performed analysis allowed revealing optimum range of iodine in drinking water associated with minimum manifestation of endemic thyroid disease and therefore its minimum risk related to water iodine.

Keywords: iodine, selenium, drinking waters, endemic goiter, geochemical health risk.

УДК: 550.4

Иод и селен в природных водах как фактор риска проявления эндемических заболеваний щитовидной железы (обзор)

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Иод – микроэлемент, необходимый для производства гормонов щитовидной железы (ЩЖ), которые регулируют развитие и функционирование живых организмов. Таким образом, его содержание представляет собой наиболее важный фактор, ответственный за эндемические заболевания ЩЖ, поскольку как недостаточное, так и чрезмерное потребление может вызвать расстройства этого органа. Согласно многочисленным исследованиям, возникновение патологий ЩЖ может быть связано с дефицитом других микроэлементов, таких как селен, который также участвует в метаболизме тиреоидных гормонов. Несмотря на то, что согласно обычным оценкам рациона, поступление иода с водой не превышает 5–10% от его общего поступления, водорастворимые компоненты имеют более высокую физиологическую ценность. Поэтому имеет смысл рассматривать содержание иода и селена в питьевой воде в связи с эндемической патологией ЩЖ. Представлен обзор научных публикаций, посвящённых исследованию содержания иода и селена в водах, в аспекте их влияния на развитие дисфункций ЩЖ вплоть до распространения эндемического зоба среди населения. Проведённый анализ показал, что концентрация иода в природных (питьевых) водах может использоваться при оценке иодного статуса территорий в отношении дефицитности или избытка иода как фактора риска распространения заболеваний ЩЖ. Согласно публикациям, распространённость заболеваний эндемическим зобом повышается в случае низкого или высокого содержания иода в питьевых водах, совместного низкого содержания иода и селена, а также при одновременном низком содержании иода в водах, почвах и растительной продукции. На основании литературных данных выявлен интервал оптимально благоприятного содержания иода в питьевых водах, при котором наблюдаемый уровень эндемических заболеваний ЩЖ минимален.

Ключевые слова: иод, селен, питьевые воды, эндемический зоб, риск заболеваний.

Iodine is an indispensable component of thyroid hormones that play a fundamental biological role controlling growth and development of organisms [1]. Natural iodine deficiency is considered as the main geochemical factor contributing to manifestation of various endemic pathological states of the thyroid gland and the goiter in particular [2, 3].

Selenium is involved in the metabolism of thyroid hormones as well [4, 5]. In case of iodine deficiency thyroxine (T4) and triiodothyronine (T3) production decrease and thyroid gland enlarges in size to obtain more iodine that is observed as goiter.

That is why in the most part of publications devoted to the identification of the origin of endemic goiter and other pathologies of thyroid gland, both trace elements are considered together [6, 7].

In the history of iodine deficiency studies there was a significantly long period of time when water as a source of iodine in diet was not paid much attention to, the focus was on products relatively enriched in this element, i.e. seafood (seaweed and fish), vegetables and eggs. The considered intake of iodine with water does not exceed 5–10% [8, 9]. Nevertheless, water and water contained in fresh food are better digested and have a higher physiological value. Therefore water iodine problem attracted more attention and the number of papers devoted to investigation of relationship between the chemical composition of natural waters, mainly iodine content in relation to endemic thyroid diseases, is nowadays progressively increasing [10–13].

The main aim of the present study is to review and analyze results of the studies on relation between the chemical composition of natural waters, primarily iodine and selenium in natural waters, and the prevalence rate of endemic thyroid diseases, i.e. publications that allow treating iodine and selenium of natural waters as natural geochemical factors provoking in certain concentration the thyroid dysfunction.

Iodine in drinking waters as an indicator of iodine transfer to human organism. The first idea of relation between endemic goiter and insufficient iodine content in drinking waters dates back to the middle of the 19th century. The studies of Prevost (1848), Chatin (1852) and Bauman (1895) contributed to accumulation of data in favor of this theory, which, however, was not recognized due to the lack of a consistent evidence base in those times. Later, in the other independent studies including those widely performed in the former USSR proved that manifestation of a pronounced endemic goiter among the local population is more typical for regions with significant iodine deficiency in soils and other environmental objects, including drinking waters. Recent studies showed that excessively high concentration of the element in natural water can also cause similar thyroid malfunction (Table 1).

Studies of iodine in natural waters and thyroid disease in the former USSR and Russia. The first studies of endemic thyroid diseases in relation to iodine content in drinking water have been performed in the former USSR in iodine-deficient mountain regions. Thus, research was performed in Kabardino-Balkaria, where until 1933 there was a maximum occurrence of endemic goiter among the population (32%) [17]. They established a very low iodine content in local natural waters, which did not exceed 0.1 μg/L.

It should be noted here that primarily used chemical method of quantitative iodine determination in water and in other types of natural objects [25] have been later substituted by the other ones. The former method slightly underestimated iodine concentration as compared to the later developed kinetic colorimetric spectrophotometer techniques (cerium-arsenic [26] and rhodanide-nitrite [27]). Nevertheless, the primary information obtained by Dragomirova technique reflected general trends of dependence between the considered parameters. The kinetic approach is still successfully used in iodine determination together with new instrumental ones (gas-liquid chromatography [28], high-performance liquid chromatography [29], voltammetry [30], ICP-MS [31], NAA [32]). A recent publication confirmed a high repeatability of I concentration values detected in urine by kinetic and ICP-MS techniques [33].

The iodine status of different areas based on the content of this element in natural waters from different sources was evaluated in the studies [34–41]. The studies have shown that the

Table 1

Levels of iodine in soils and waters of different regions in association with endemic goiter

Country, region	Iodine in soils (mg/kg)	Iodine in water (μg/L)	Endemic goiter (%)	Reference
New Zealand	0.3	–	62	[14]
	0.4	–	40	
	3.2	–	19	
	11.2	–	4	
	14.0	–	7	
Switzerland	0.62	–	56	[15]
	1.40	–	61	
	4.94	–	12	
	11.9	–	1	
New Zealand (Taranaki)	14.0	–	4	[16]
New Zealand (Auckland)	12.0	–	4	
Kabardino-Balkaria	–	0.1	32	[17]
Russia, Dagestan, Stanislav region	0.3–0.35	–	III–IV degree	[18]
	0.45–0.65	–	lower than III degree	
Central China	–	462.5	65	[19]
	–	54.0	15.4	
Sri Lanka (Wariyapola)	9.4	–	12	[20]
Sri Lanka (Angunawala-Daulagala)	1.9	–	45	
Sri-Lanka	3.9	7.02	10	[21]
	2.0	5.5	10–25	
	2.26	66.5	25	
India (Patharpratima)	–	100.4	> 30 (60.7*)	[22]
India (Sagar)	–	22.9	> 30 (55.8*)	
India (Namkhana)	–	68.4	> 30 (43.9*)	
India (Basanti)	–	53.5	20.0–29.9 (25.9*)	
India (Gosaba)	–	60.4	20.0–29.9 (25.1*)	
India (Lamshang)	–	2.6	> 30 (35*)	[23]
India (Wangoi)	–	1.8	> 30 (39.4*)	
India (Samurou)	–	2.2	> 30 (30.7*)	
China (Anhui)	–	252.0	11.7	[24]
China (Hebei)	–	266.0	7.9	
China(Shaanxi)	–	90.6	1.9	
China (Tianjin)	–	303.0	10.0	

*Note: *Thyroid goiter cases among children; a dash indicates the absence of data.*

concentration of iodine in the local river runoff can be an important criterion of iodine supply in certain areas.

At the same time, the established values of the minimum iodine content in waters possibly causing contributing to manifestation of endemic goiter varied considerably in different regions. According the data obtained in Ukraine in sixties of the last century [34], a severe degree of thyroid endemia among population was observed in areas where the average iodine content in surface and groundwater was as low as 1–2 μg/L; moderate manifestation of the disease was registered at the range of 2 to 5 μg/L; and weak – at 5 to 10 μg/L I; pathology was not found when iodine content in water equaled or exceeded 10 μg/L. In studies of iodine in natural water of Almetyevsky and Leningradsky districts of Republic of Tatarstan, it was found that the minimum sufficient level of iodine equaled to 4 μg/L [35]. In the other research, it was revealed that cases of thyroid pathology were absent in regions with the element concentration in natural waters over 25 μg/L [38].

In Kazakhstan [42], as well as Tatar republic, the zone that is highly iodine deficient corresponded to iodine content in waters less than 4 μg/L; moderately deficient zone– to iodine level from 4 to 10 μg/L and the relatively sufficient zone was characterized by iodine level exceeding 20 μg/L.

Recent study [12] established that iodine content in the drinking waters of the city of Bratsk, which is located in areas with a high incidence of iodine-deficiency diseases, is only 0.2 μg/L, this level being associated with a severe degree of thyroid goiter pathology. In this area the low iodine content in local waters was accompanied by the low level of the element in food.

High negative correlation (r = -0.98) between iodine level and occurrence of thyroid endemic diseases was established in some regions of Dagestan [41]. The mountainous area is characterized by both low iodine and selenium amount in natural waters (2.0–2.8 μg/L and 1.4–1.7 μg/L respectively), related to the low elements' content in atmospheric precipitation and soils (2.1–2.4 μg/L iodine and 0.08–2.16 μg/L selenium) and vegetation (0.15–0.40 μg/L iodine and 0.009–0.02 μg/L selenium).

Studies of iodine and selenium in water in relation to thyroid disorders in the other countries of the world. The first studies of iodine deficiency in Europe have been described above. In the middle of the last century, this problem was studied in the countries of Asia and Africa. D. Wilson [43] associated the prevalence of goiter in Sri Lanka with the iodine content in drinking water in the range of 1.4–2.7 μg/L. Later studies in this country [44] showed that in areas where a high degree of thyroid pathology were observed iodine level in drinking water varied from 2.2 to 10.1 μg/L, and in areas where goiter was not detected, the concentration iodine in waters ranged from 19.4 to 183 μg/L. The authors concluded that the local level of the threshold iodine concentration is 10 μg/L. Egyptian scientists found that iodine concentration of 7 to 18 μg/L in the drinking water of New Valley oases caused development of goiter among the inhabitants of the oases, while the iodine content from 44 to 100 μg/L excluded the disease cases [45]. In areas of endemic goiter in the mountainous part of eastern Ghana, the average iodine amount in waters did not exceed 10 μg/L [46]. Thus, in a number of studies conducted in different countries, the concentration of 10 μg/L of iodine in drinking water may be treated as a lower threshold.

Comparatively recently the territory of Denmark was zoned according to the iodine status basing on an assessment of the trace elements and iodine content in drinking water with identification of potentially deficient, optimal and excess of iodine [47]. Another study of drinking water from centralized water supply in Denmark revealed that groundwater was the main source of iodine intake in local diets [48]. To build a spatial model with different levels of iodine concentration in waters and to identify natural factors and water types in particular, influencing the intake of iodine into the human body they used cluster analysis. It was shown that the iodine content in drinking water was determined by both the natural (geological) and technological factors (the preliminary treatment of water before it was supplied to the residues). Estimation of the contribution of drinking water to provision of iodine to residents showed that intake of iodine by adults may exceed the WHO-recommended average daily level (150 μg), while in teenagers' diets iodine provision with drinking water varies from 0 to 50% of the established standard. The authors paid attention to local changes in micronutrients' supply and recommended taking this into account when approving various programs for food products iodizing. Even at low content of iodine in drinking water in most cases, distribution of the halogen in waters of various hydrogeological structures is different and should be accounted of in case of their usage by local population.

On the other hand, Chinese researchers have revealed that a high iodine content in drinking water may stimulate the development of endemic goiter among the population as well [49]. A large-scale survey of 1978 cities in 11 provinces of China with a sampling of 28.857 water samples showed that the iodine content ranged from 150 to 300 μg/L, and the authors concluded that the incidence of goiter increased with an increase in iodine concentration in drinking water (Fig. 1). Therefore, there exists also the upper threshold for iodine concentration in drinking water, which lies in the range of iodine concentration from 250 to 300 μg/L. Above this level an increase of goiter among the children corresponded to increase of iodine in drinking water.

In accordance with classification [42] the regions with a moderate iodine deficiency in India are characterized by the average iodine level in drinking water varying from 4 to 10 μg/L [11].

A comparison of chemical composition of 609 water samples collected in 8 districts of Sri Lanka and the data on the incidence of endemic goiter among local population allowed to conclude that low manifestation of the disease corresponded to the mean iodine concentration in water equaling to 92.8 μg/L (n = 135), while the

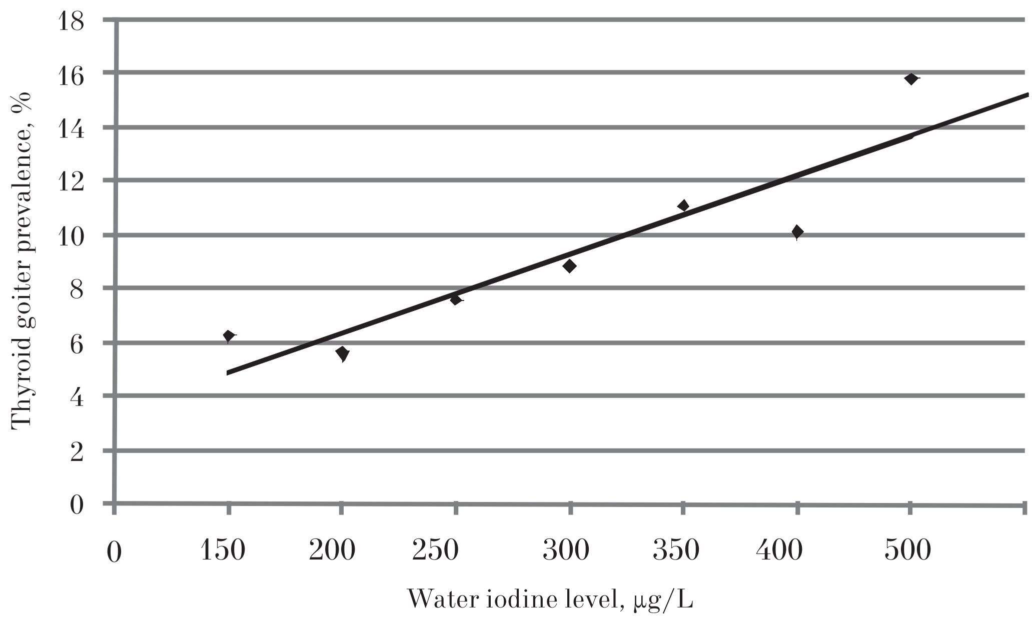

Fig. 1. Relationship between water iodine level (µg/L) and goiter prevalence (%) among children aged 8 to10 years (the data from [49])

Table 2

Iodine and selenium concentration in water samples collected in Kalutara (Sri Lanka, after [13]

DS division	Water source	Iodine concentration, µg/L	Selenium concentration, µg/L	Goiter patients
Bulathsinghala	Surface water	23	< 1	No
	Dug well	62	< 1	Yes
	Tube well	20	< 1	No
Ingiriya	Dug well	9	5	Yes
	Surface water	31	< 1	No
	Dug well	24	< 1	Yes
Panadura	Surface water	40	< 1	Yes
	Dug well	27	< 1	Yes
	Dug well	61	< 1	No

highest level of the disease corresponded to water mean iodine content of 25.3 µg/L and lower (n = 284) [50]. Rank correlation calculated between iodine concentration in drinking water and the incidence rate of the disease among habitants equaled to -0.64.

The study of endemic goiter prevalence in the same region (Kalutara) has been performed also in the framework of the World Health Organization program concerning salt iodination [13]. According to the results of this study the average iodine concentration in ground water from the endemic goiter regions was 28.25±15.47 µg/L. The non-goiter regions had almost similar content of iodine in the drinking ground water (24.74±18.29 µg/L) while in the surface waters iodine concentration was on the average slightly higher (30.87±16.13 µg/L). One should note significant variation of mean iodine values in both regions (52–74%) that shows their considerable heterogeneity in this parameter. Selenium content practically in all of the examined water samples did not exceed 1 µg/L showing no definite correlation with the thyroid goiter frequency (Table 2). However, the authors reported that endemic goiter was detected in some isolated localities where both iodine and selenium levels were low, concentration of the latter being below 10 µg/L. In addition, the study showed that some other geochemical parameters such as soil pH, organic matter content and/or thick lateritic cap control activity of selenium and iodine transfer to food chain through plant uptake and water in endemic goiter area. Thus, for example, a decrease in the selenium bioavailability and, consequently, its lower intake into living organisms, is facilitated by a high content of organic matter, acid sulfates, iron and aluminum in the soils of the Kalutara.

Influence of the other factors on the occurrence of iodine deficiency. Indeed, there are cases and direct evidence of additional risk of endemic thyroid diseases in areas where natural iodine deficiency is accompanied by man-made pollution. The most evident example is a nuclear accident, when technogenic radioactive isotopes of iodine enter the atmosphere. If radioiodine falls out in regions with a low stable iodine status, the risk of endemic thyroid diseases, including cancer, increases. Given a high mobility of iodine, it is possible to assume a rapid involvement of iodine radioisotopes in food chains due to easy transfer in food chain to pasture plants, milk and then the human body. The studies performed in the zone of radioactive fallout after the accident at the Chernobyl nuclear power plant showed a significant increase in thyroid cancer cases among children who lived in the period of deposition in contaminated areas of Belarus, Russia and Ukraine [51–53]. A combined effect of iodine deficiency and radioactive contamination is considered as a possible cause of thyroid cancers studied also in Turkey [54].

Our studies of drinking water collected in the private farms located in the Bryansk region affected by the Chernobyl accident confirmed low water iodine content. Therefore, we suggested that it might contribute to the risk of thyroid diseases caused by iodine radioactive isotopes [55]. Iodine concentration in drinking waters was compared with their chemical composition, as well as with the types of water-bearing soils and rocks, and the content of typomorphic macroelements (H, Ca, Fe), defining classes of water migration, mobility of trace elements [56] and, accordingly, their transition to food chains. Iodine content in the drinking waters of the surveyed households did not exceed 10 μg/L, i. e. the level, which, according to the published data, corresponds to the lower threshold iodine concentration in drinking water. In addition, the studied water samples had a low concentration of selenium. Enhanced level of iodine was detected in surface and groundwater in the areas of loess-like loamy deposits (median values 16.6 and 10.1 μg/L) [57, 58]. Similar to iodine, the groundwater in these areas turned out to be comparatively enriched also in selenium (0.72 μg/L) [59].

Finally the analysis of publications devoted to iodine and selenium studies in waters as a factor contributing to occurrence of endemic thyroid diseases showed that the incidence rate of these pathologies correlates not only with low but also with high iodine content in drinking water. These facts allowed us determining both the upper and lower threshold iodine concentration range in drinking water with revealing the optimum iodine content associated with minimum rate of the thyroid endemic morbidity. According to the analyzed data the lower threshold concentration of iodine considerably varies in different countries of the world from 0.1 to 10 μg/L, the cause of which requires additional research. A moderate manifestation of endemic goiter is observed in regions with the iodine content in drinking water at a level within a range of 4–10 μg/L. The upper threshold concentration is likely to correspond to the interval of 250–300 μg/L (Fig. 2), and for children this threshold lowers to 200 μg/L (Fig. 1). Further increase of iodine amount in drinking water leads to a corresponding growth of the rate of endemic goiter incidence. Therefore the optimum concentration of iodine content in drinking water, at which there a minimal incidence of thyroid has been observed lies between 10–50 μg/L and 200–250 μg/L (depending on the region and population, Fig. 2).

Conclusions

Analysis of the published and our original data shows that the iodine and selenium in drinking water are the important factors that may provoke the risk of thyroid endemic diseases among local population including endemic thyroid goiter. Performed review made it possible to analyze and establish the upper and lower threshold intervals of iodine concentration values in drinking water, below and above which an increase in the incidence of endemic goiter is observed. The interval between these threshold values present the optimum iodine range at which the risk of endemic goiter occurrence is minimal.

It is also shown that in areas with iodine deficiency subjected to fallout of radioactive iodine isotopes, the risk of thyroid morbidity increases due to the combined effect. Further studies clarifying the threshold level of iodine in drinking water, plants and soils in various territories for different groups of population, as

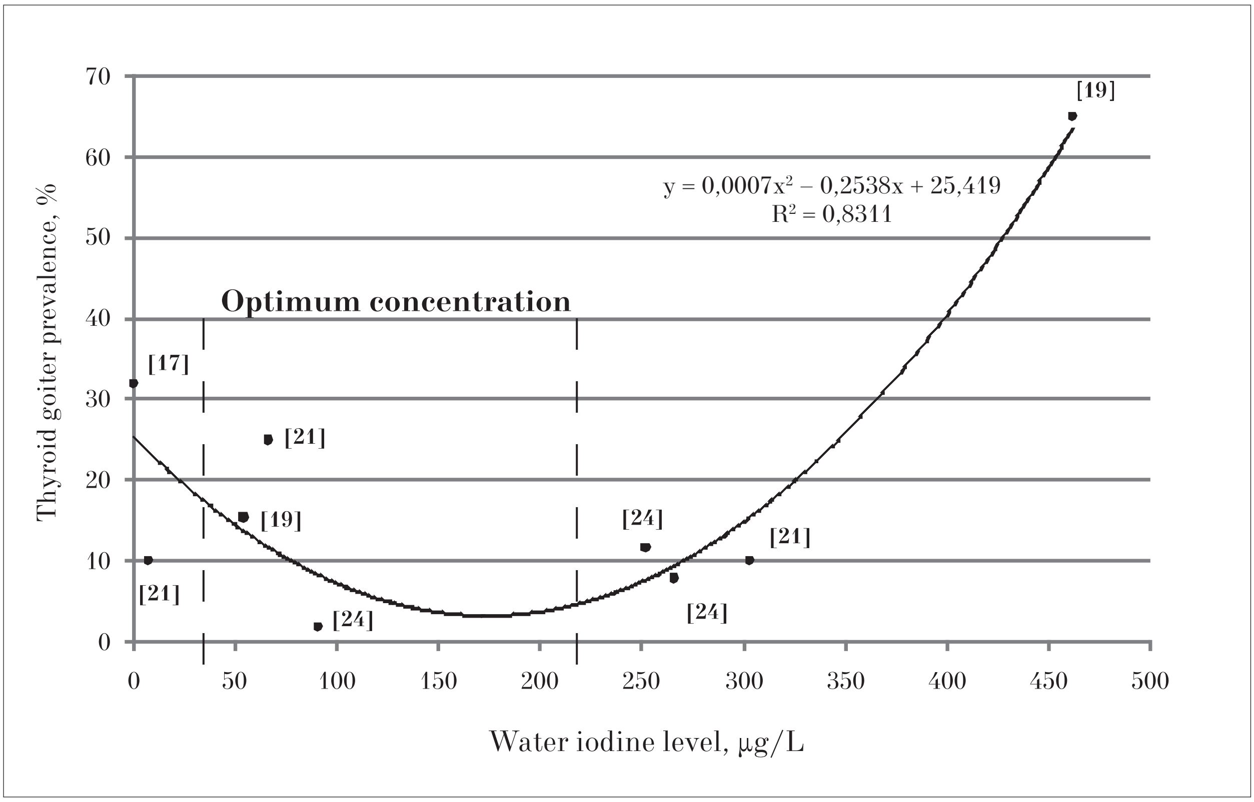

Fig. 2. Relation between iodine concentration in drinking water and thyroid goiter prevalence

well as determination of a combined contribution of deficiency or excess of iodine and selenium to the risk of endemic thyroid diseases are the promising and practical fields of investigation.

The results of such studies will not only significantly improve the effectiveness of monitoring and prophylactics of widespread thyroid diseases and improve the quality of life, but also significantly improve the health state of the population.

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