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EPIDEMIOLOGICAL INDICATOR VALUE IN THE IODINE AVAILABILITY ASSESSMENT — EVIDENCE FROM THE REGIONS OF THE RUSSIAN FEDERATION

Abstract

Background: In the Russian Federation, newborn screening comprises thyroid stimulating hormone determination to exclude primary congenital hypothyroidism. Screening is carried out throughout Russia. Neonatal TSH can be used to assess iodine deficiency and monitor iodine prevention programs.

Objective: To assess and compare official statistical data on congenital hypothyroidism, the prevalence of hypothyroidism and iodine deficiency syndrome in children, as well as urinary iodine in the Russian regions.

Materials and methods: The level of neonatal TSH was determined in 97.69% of children born in the Russian Federation in 2017. This article represents the results on the prevalence of hypothyroidism in the regions with various iodine availability. The correlation analysis was used to assess the relationship of CH incidence in newborns and iodine availability.

Results: The calculated correlation coefficient, which was 0.2, reflects a weak relationship between the degree of iodine deficiency in the region and the number of newborns diagnosed with congenital hypothyroidism.

Conclusions: In the Russian Federation, a law on universal salt iodization does not exist, and many regions are still in conditions of moderate or severe iodine deficiency. To assess the iodine status in these particular regions, we could use the results of newborn TSH screening.

Key words: *congenital hypothyroidism, newborn screening, iodine deficiency, thyroid-stimulating hormone*

Conflict of Interests

The authors declare no conflict of interests.

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Search and analytical work on the preparation of the manuscript was carried out as part of the state task: a scientific assessment of the need for additional regulatory and other measures to eliminate iodine deficiency in pilot regions with severe iodine deficiency.

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CH — congenital hypothyroidism, IDD — iodine deficiency disorders, Me — median, fT4 — free thyroxine, TSH — thyroid stimulating hormone

Introduction

Iodine deficiency, detected in the environment, as well as related disorders (IDD) form a wide range of medical and social problems around the world due to high prevalence and serious clinical consequences [1].

Newborn screening for thyroid-stimulating hormone is carried out throughout the Russian Federation.

Based on these results, we can assume the presence of factors in this environment that affect the thyroid, namely the availability of iodine. In newborns, pituitary thyroid-stimulating hormone (TSH) is inversely related to the level of urinary iodine [2]. The results of newborn screening for hypothyroidism are used to assess the prevalence and severity of iodine deficiency disorders [3]. Maternal iodine deficiency is the most common cause of increased TSH levels in infants in iodine-deficient areas. In 1994, the World Health Organization (WHO) established criteria for neonatal hyperthyrotropinemia for regions with mild, moderate and severe iodine deficiency. According to the recommendations, neonatal TSH levels above 5 μIU/L are determined in no more than 3% of newborns in areas with high iodine availability, in regions with mild iodine deficiency this figure is 3–19.9%, with moderate — 20–39.9% [4]. For those countries where the universal salt iodization program is implemented, newborn screening may be a relevant indicator of iodine deficiency and related diseases. Neonatal TSH above 5 μIU/L has financial advantages for the assessment of iodine deficiency, because it covers all newborns in this area, and does not require additional studies [5]. Iodine deficiency is the most common but preventable cause of mental retardation worldwide. This condition can be prevented if you start taking iodine prophylactically before pregnancy [6]. The problem of endemic cretinism is of high relevance for regions with severe iodine deficiency.

Objective

To evaluate and compare the official statistics on congenital hypothyroidism, statistical reporting of the prevalence of hypothyroidism and iodine deficiency syndrome in children, as well as urinary iodine in the regions of the Russian Federation.

Materials and Methods

Study Design

The study was conducted using statistical data received from FSBI Research Centre of Medical Genetics (data of federal screening for congenital hypothyroidism). The Table presents the number and percentage of children with TSH >20 μU/mL. Data on the incidence of hypothyroidism in older age and congenital iodine deficiency syndrome were obtained from f. 12 of Rosstat of Russia. Data on median urinary iodine were obtained from studies conducted by FSBI Endocrinology Research Centre of the Ministry of Health of Russia in the regions of the Russian Federation. The study is observational, continuous, and multicenter.

Eligibility Criteria

The study enrolled 97.69% of all newborns (in absolute numbers — 1 632 801 newborns) in the Russian Federation in 2017. In addition, children and adolescents in the Russian Federation, male and female, living in different regions of the Russian Federation and suffering from diseases primarily caused by iodine deficiency in the diet were included.

Description of Medical Intervention

Determination of thyroid-stimulating hormone in a whole-blood sample of newborns was carried out via immunofluorescence method using DELFIA Neonatal TSH reagent kit (PerkinElmer, Inc., USA.) The threshold value for the detection of congenital hypothyroidism was TSH >20 μU/mL. At the stage of primary screening congenital and transient hypothyroidism was not differentiated, but it can be noted that transient hypothyroidism is accompanied by relatively high levels of TSH (9–40 of μU/mL) than congenital one (TSH level in most cases is more than 40 μU/mL). Such conditions can be distinguished at the 2nd stage of screening in outpatient settings by detecting serum TSH and fT4 [6].

Subgroup Analysis

Patients were divided into two groups according to age: newborns and children under 14 years. Prevalence is estimated for the following diseases (statistical reporting names are presented in accordance with ICD-10): congenital iodine deficiency syndrome, subclinical hypothyroidism due to iodine deficiency and other forms of hypothyroidism.

Ethical Review

The Local Ethical Committee of FSBI Endocrinology Research Centre of Ministry of Health of Russia approved this study on 13.02.2019.

Statistical Analysis

Sample size calculation principles: The study was conducted on the principle of a continuous, rather than a sample study, which may be justification for not calculating the minimum sample size.

Methods of statistical data analysis: To assess the relationship between the number of newborns diagnosed with CH in regions with different iodine levels, a correlation analysis was performed using the non-parametric Spearman method. The correlation coefficient for median urinary iodine and percentage of newborns with CH was calculated using Statistica data analysis software system, version 13, TIBCO Software Inc. (2017). This correlation coefficient r is significant for $p < 0.05000$

Results

Data on the sample of patients were obtained on the basis of official statistics. The sample included persons of both sexes living in different regions of the Russian Federation.

Table 1 presents the results of comparing data on the incidence and prevalence of hypothyroidism in different regions of the Russian Federation with different iodine availability. In these regions, epidemiological studies were conducted jointly with FSBI Endocrinology Research Centre of the Ministry of Health of Russia.

Table 2 presents the results of statistical processing.

The calculated correlation coefficient, which was 0.2, reflects a weak relationship between the degree of iodine deficiency in the region and the number of newborns diagnosed with congenital hypothyroidism. This may be due to various factors. First, attention is drawn to possible inaccuracies in official statistics, which is seen in the analysis of the number of newborns with CH and the number of children 0–14 years old diagnosed with hypothyroidism.

Discussion

Discussion of Main Study Result

Newborn screening for TSH is primarily aimed at detecting congenital hypothyroidism due to congenital thyroid dysgenesis and, in rare cases, genetic factors. For the assessment of iodine availability in the regions, it may be necessary to use a more sensitive indicator, for example, neonatal TSH >5 μU/mL. However, as many neonatal TSH studies have shown, newborn screening may be useful for detecting moderate to severe iodine deficiency, but should be cautiously recommended for assessment in regions with mild iodine deficiency. For example, in Georgia, where Me of urinary iodine is 297 μg/L in schoolchildren and 211 μg/L in pregnant women, in some areas, the percentage of newborns with TSH >5 μU/mL was 4.4%, which can be falsely interpreted as moderate iodine deficiency [7]. In Austria, despite the relatively low median of urinary iodine (85 μg/L in pregnant women), the percentage of newborns with elevated TSH levels was much lower — 2.2% [8]. In Belgium, there is a mild iodine deficiency in pregnant women, but the incidence of increased

Table 1. Data on congenital hypothyroidism and urinary iodine in the Russian regions

Regions	Urinary iodine median (μg/L) [min; max]	Number of newborns	CG (abs)	CG (%)	Hypothyroidism incidence (0–14)	Congenital iodine deficiency syndrome (0–14)
Moscow	104.5 [70.9; 135.5]	128,826	67	0.05	0	0
Moscow Region	74.2 [47.3; 129]	84,448	41	0.04	783	103
Belgorod Region	57.3 [49; 86.0]	14,918	3	0.02	281	302
Ivanovo Region	105.4 [36; 624]	10,320	1	0.009	42	3
Kaluga Region	66.2 [46.3; 94.2]	10,720	5	0.04	52	7
Smolensk Region	61 [12; 400]	8,560	2	0.023	102	7
Ulyanovsk Region	81.9 [58.9; 156]	11,901	2	0.016	714	12
Voronezh Region	152.4 [69.8; 209]	22,550	8	0.035	421	21
Komi Republic	57.2 [43.1; 108]	9,484	2	0.021	228	12
Murmansk Region	41.6 [4.7; 68.4]	7,715	2	0.025	259	2
Arkhangelsk Region	63.7 [39; 84]	11,502	3	0.026	94	1
Volgograd Region	52.8 [38.9;79]	24,512	2	0.008	447	13
Astrakhan Region	25.9 [18.8; 32.2]	12,189	4	0.03	60	0
Krasnodar Region	79.3 [47.3; 126]	65,942	22	0.03	741	149
Kabardino-Balkaria	141.1 [109; 168]	9,234	2	0.021	179	32
Republic of Tatarstan	72.1 [46.9; 88.9]	48,120	15	0.03	805	172
Udmurtia	68.3 [30.8; 125]	17,903	11	0.06	189	10
Chuvash republic*	38.2 [6.8; 250]	14,044	1	0.007	180	0
Penza Region	70 [23; 308]	11,836	1	0.008	494	17
Nizhniy Novgorod Region	70.9 [46; 129]	33,575	13	0.03	210	0
Kirov Region	65.9 [43.8; 101]	13,503	8	0.05	683	0
Perm Region	95.5 [16.3; 351]	31,663	7	0.022	1137	29
Sverdlovsk Region	96 [55; 144.7]	53,443	14	0.026	1339	39
Khanty-Mansi Autonomous Area	229.7 [5.6; 837]	22,752	7	0.03	1396	54
Tuva Republic	123 [23; 436]	6,989	3	0.04	165	15
Samara Region	100.8 [23; 326]	34,258	10	0.029	684	47

*iodine deficiency of moderate severity according to Me of urinary iodine

Table 2. Statistical data

Indicator	Result
r — correlation coefficient	0.261
ρ — validity of the correlation coefficient	0.198
t — significance of the correlation coefficient	4.98

TSH during follow-up was low, and the authors also note a low sensitivity of this indicator for populations with mild iodine deficiency or optimal iodine intake [9]. In the regions of the Russian Federation, studies on the possibility of using neonatal TSH as a marker of iodine deficiency were also conducted. In the Tyumen Region the TSH levels of above 5 μU/mL were analyzed. According to the results of the study, a reduction in the rate of hyperthyrotropinemia up to 5% was shown, which indicates an improvement of the iodine status on the back of preventive measures. Analysis of various parameters of iodine deficiency severity showed that in the region with iodine prevention among pregnant women, monitoring of iodine deficiency disorders via hyperthyrotropinemia detection is limited to pregnant women themselves, because the iodine consumption is monitored in this group only [5]. In the Krasnoyarsk Region, TSH levels in the whole blood of newborns were analyzed. The rate of neonatal TSH >5 μU/mL corresponded to mild iodine deficiency and moderate one in some regions, which generally reflects the improving iodine availability in regions with severe environmental iodine deficiency [10]. A study conducted in Moscow found that with the implementation of measures to prevent iodine deficiency, the rate of neonatal hyperthyrotropinemia significantly decreased and amounted to 0.44% in 2000 and 0.60% in 2006 [11]. Considering all the above, neonatal TSH above 5 μU/mL can be used to assess iodine status in pregnant women in a population with moderate and severe iodine deficiency. For the general population, in future it is possible to assess thyroglobulin in both newborns and school-age children as a marker of iodine deficiency in the regions [12]. Thyroglobulin is negatively associated with urinary iodine and significantly elevated in children with severe iodine deficiency. Since there are practically no anti-thyroglobulin antibodies in children, its concentration may reflect the true pattern of iodine deficiency in the region [13].

Study Limitations

It is impossible to completely exclude the human factor when assigning a diagnosis according to ICD-10, which can significantly distort the statistical reporting data.

Conclusions

The level of thyroid stimulating hormone in newborns may be a sensitive marker of iodine deficiency when using a threshold TSH level >5 μU/mL. TSH >20 μU/mL should be used to detect primary congenital hypothyroidism associated with genetic factors. Given the absence of a law on universal salt iodization in Russia, many regions are still in conditions of moderate or severe iodine deficiency, and the use of newborn screening for TSH in these regions is possible to assess the iodine status of the population. In regions with mild iodine deficiency or optimal iodine availability, it is necessary to use other markers, including thyroglobulin.

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