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Structural – functional Characteristic of the Thyroid Gland During Various Periods of Embryonic Development of Goitrous Endemia, on the Example of the Republic of Sakha (Yakutia)

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ABSTRACT
Morphometric indices, structural components in fetuses and newborns were studied depending on gestation and morphofunctional variant. The object of the study was 130 thyroid glands obtained from fetuses and deceased newborns, from 22 full to 40 weeks of gestation. The average thyroid volume in fetuses and newborns in the Republic of Sakha (Yakutia) exceeded the thyroid volume of the non-endemic iodine in the region of St. Petersburg. The morphofunctional activity of the thyroid gland in children of the early and late neonatal period, compared with data from the iodine-non-edemic region, remains high and indicates a delay in morphological differentiation of the fetal gland in the focus of iodine insufficiency. It was revealed that stromal structural components of the gland are more pronounced in fetuses and newborns of Yakut nationality, and in children of Russian nationality had structural components of parenchyma.

Keywords: *thyroid gland, embryonic development, goitrous endemia, Republic of Sakha, Yakutia*

1. INTRODUCTION

The Republic of Sakha (Yakutia) belongs to territories with high iodine deficiency in nature and is characterized by high prevalence of thyroid pathology among both child and adult population.

According to studies conducted by the "National Medical Research Center of Endocrinology" of the Ministry of Health of the Russian Federation together with the International Council for the Control of Iodine-Deficient Diseases, the prevalence of endemic goiter in children and adolescents in the central part of Russia is from 15 to 25 %, and in the Republic of Sakha (Yakutia) this indicator reaches up to 39 % [1]. In addition to the lack of iodine and a number of other trace elements in the environment, a number of specific features of Yakutia affect the body as a whole and in particular the thyroid gland (thyroid gland): extreme temperature and light conditions, pronounced seasonality of the climate, anomalies of geomagnetic fields [2].

The thyroid gland development in fetus occurs in direct dependence on the functional state of the mother's thyroid gland, therefore, the influence of the same pathological signs that affect the state of the mother's gland is natural. At the same time, according to the state report of population health of the Republic of Sakha (Yakutia), thyroid pathology ranks third in the pattern of incidence of pregnant women. Pregnancy exacerbates iodine deficiency, due to the increased need of the body for thyroid hormones and iodine loss due to increased renal clearance. Iodine deficiency, causing hypotyroxinemia, leads to excessive thyroid stimulation, on the background where hyperplasia of the fetal thyroid gland and the development of iodine deficiency disease is.

In addition to the lack of iodine and a number of other trace elements in the environment, the body as a

whole and in particular the thyroid gland is affected by a number of specific features of Yakutia: extreme temperature and light conditions, anomalies of geomagnetic fields.

Currently, some ethnic features of physical and sexual development have been established among the population of the Republic of Sakha (Yakutia) [2]. However, thyroid ontogenesis studies different ethnic groups living in the same climatic-geographical region of the Republic

Purpose of the research is to establish morphofunctional features of the thyroid gland in fetuses and newborns in the goiter-endemic region, on the example of the Republic of Sakha (Yakutia).

2. MATERIALS AND METHODS

The subject of the study was 130 thyroid glands of fetuses and deceased newborns from 22 full to 40 weeks of gestation. Autopsies and sampling of material were carried out within 24 hours from the moment of death of fetuses and newborns in the pathological department of the republic hospital No. 1 of Yakutsk. There were: boys – 72, girls – 58; stillbirths – 51, live births – 79, died in the early neonatal period – 59 of them (45.4 %), in the late neonatal period – 20 (15.4 %); by ethnicity: Yakuts – 73 (56.1 %), Russians – 57 (43.8 %). Material grouping was done depending on the gestation period – 22–27, 28–32, 33–36, 37–40 weeks of intrauterine life. According to accepted WHO criteria (1999), fetuses and newborns 22–27, 28–32, 33–36 weeks of gestation belong to the group of preterm babies, and they are full-term from 37 weeks of intrauterine development. The entire sample is represented by 130 pathological studies. We studied the birth history and development of the newborn, individual cards, case histories, autopsy protocols for stillborn and deceased newborns. Ethnicity was determined by phenotypic features and indicated nationality in the mother's history.

The topography, shape, absolute (g) and relative weight of the thyroid gland were determined. The length, width, height of the gland lobes were measured. To determine the dynamics of thyroid development, gland volume indicators were calculated, which were correlated with the size and weight of this organ [3, 4]. The thyroid volume of the lobes was determined by Brunn formula. The individual thyroid volume norm was calculated by body weight. For histological examination, serial sections with hematoxylin and eosin staining were carried out. Type of morphofunctional state of thyroid gland was evaluated by gestation period, mean thyroid follicle diameter, mean thyroid cell height, mean thyroid cell core diameter, relative volume of follicular epithelium, interphollicular epithelium, colloid, stroma and vascular bed were determined [3, 5].

Statistical processing of the results was carried out with the Student's t-test by the statistical program "Statistika 6.0."

3. RESULTS AND DISCUSSION

Some researchers [3, 4, 6] described the originality of the thyroid gland of the fetal and neonatal periods that was reflected in morphofunctional state change. A follicular-colloidal type of structure indicating moderate functional activity is distinguished, as well as mixed (transient) and desquamative types observed with high functional tension of the thyroid gland.

The morphofunctional state of the thyroid gland – the proportion of the desquamative type was 48.4 %, which was 2 times more than the follicular-colloidal (25.3 %) and transient (26.1 %) types.

The comparative assessment of O.K. Khmelnitsky and A.Yu. Ivanova's data in the non-edemic region of St. Petersburg, [4] showed that the functional activity of the fetal gland in children of the early and late neonatal period of Yakutia did not decrease, but remained high at the late stages of gestation.

Thyroid volume indicators for all gestation periods in the endemic region exceeded non-endemic region data (Figure 1). Thyroid volume in fetuses and newborns in the endemic region was 0.054 + 0.003 %, in the non-endemic region – 0.049 + 0.002 %.

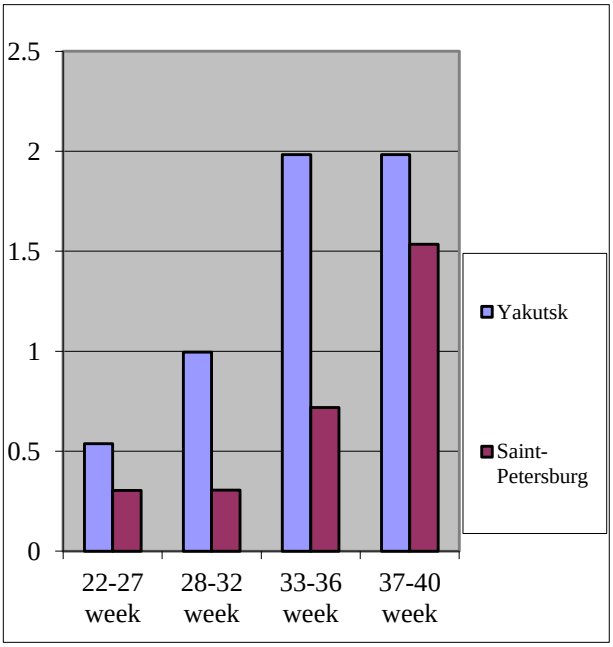

Figure 1. Mean thyroid volume (in cm3) according to gestation period

Comparison of actual thyroid volume with thyroid volume norm boundaries by life periods showed that, the actual thyroid volume was closer to the upper thyroid volume norm boundary at 22–27, 28–32, 33–36 weeks, in the stillborn and neonatal group of the early

neonatal period, while the actual volume at 37–40 weeks went beyond the norm (in stillbirths at 0.315 ml, in newborns of the early neonatal period at 0.352 ml) (Figure 2). The actual thyroid volume greater than the upper limit of the norm was noted in 31.5 % of fetuses and newborns.

Thus, the signs of high functional tension, high thyroid thyroid volume in fetuses and newborns of Yakutia are probably associated not only with the features of the adaptation mechanisms of the fetal period, but also with the development of adaptively compensatory changes to goitrogen factors and primarily to iodine lack of a given region.

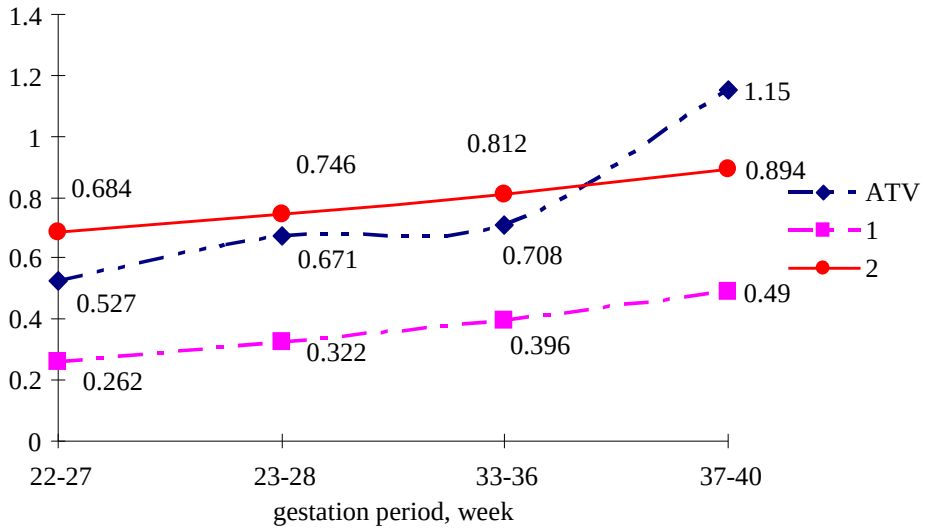

Figure 2. Actual thyroid volume (ATV) and individual thyroid volume norm depending on gestation period. Note: 1 – the upper limit is the norm of thyroid volume, 2 – the lower limit is the norm of thyroid volume

When analyzing the parameters of fetal gland lobes size according to the formed gestation terms, it was revealed that in all gestational terms, the height of both lobes of the gland was higher in children of Russian nationality, (in terms of 22–27 – $p < 0.05$), and the indicators of thickness and width of the left and right lobes were significantly lower ($p < 0.05$) than in children of Yakut nationality. Thus, in fetuses and newborns, fetal gland differed in national characteristics. This was probably due to the anthropometric features of the indigenous inhabitants of the Republic of Sakha (Yakutia).

The peculiarity of the thyroid gland of the fetal and neonatal periods is reflected in the change in the functional and morphological state. There is a follicular-colloidal type of structure, indicating moderate functional activity, as well as mixed (transitional) and desquamative types observed with high functional tension of the thyroid gland.

A morphometric study of the follicular-colloidal type of thyroid gland found that with an increase in the gestation period, the average diameter of the follicles increases with the accumulation of colloid and a decrease in the height and diameter of the nucleus of the thyroid epithelium. These indicators indicate a decrease in functional stress by the period of 37–1 weeks with the predominance of the processes of accumulation of intra-follicular colloid (Table 1).

The mixed type was characterized by a significant increase in functional activity, namely, an increase in the height of thyrocytes and the diameter of the nuclei, a decrease in the volume of the colloid, an increase in the volumes of the interfollicular epithelium and the vascular bed. Along with the follicles, there were signs of peeling of the follicular epithelium. The average outer diameter of the follicles increased by 2 times by 37–41 weeks of gestation.

The indicators of the average diameter of the thyroid cell nucleus in the desquamative state were the lowest compared to other types of thyroid, while the value of the relative volume of vessels in almost all groups exceeded the indicators of the other two types of thyroid structure.

In comparison with the non-endemic region, in Yakutia, the indicators of the relative volume of the vascular bed were almost 2 times higher. This is confirmed by experimental studies of a number of authors [5], who, in the mode of iodine deficiency, established a significant increase in the relative volume of vessels in the thyroid gland of rats due to the formation of new vessels from the stromal arteries, increasing the contact area in the thyrocyte – capillary system.

When comparing morphometric indices of thyroid structural components by ethnic characteristics, the following was established: at 22–27 and 28–32 weeks in

fetuses and newborns of both nationalities, high functional activity of the gland was recorded, which was explained by high rates of desquamative type, characterized by some reduction in gland activity compared to early life. The average diameter of the follicle, as well as the relative volume of the colloid, were largest at 37–40 weeks in children of Russian nationality, with a slight decrease in the average height of the thyreocytes, the relative volume of the interpollicular epithelium and the follicular-colloid index, which indicated a decrease in the functional tension of the fetal gland at a given gestation period with a predominance of intrafollicular colloid accumulation processes. The follicle diameter and the relative volume of follicular and interpollicular epithelium decreased within 37–40 weeks in children of Yakut nationality, with an increase in stromal and vascular volume. The relative volume of the vascular channel exceeded at all gestation periods in the Yakuts than in the Russians.

Table 1. Morphometric parameters of the thyroid gland of fetuses and newborns, depending on the gestational age

Morphometric indicators	Morph. type	gestational age, week			
		22-27	28-32	33-36	37-40
Average outer diameter of the follicle, microns	1	69.51±1.54	67.18±1.83	79.85±1.37	85.16±0.56
	2	56.94±1.81	70.17±2.02	82.42±1.5	102.5±0.73*
Height of the follicular epithelium, microns	1	9.28±0.14*	7.2±0.1	8.3±0.21	7.8±0.15
	2	8.94±0.16	9.1± 0.18	8.61±0.12	9.87±0.1
Diameter of the nucleus of the thyroid epithelium, microns	1	6.12±0.03	5.74±0.07	5.6± 0.03	4.92±0.05*
	2	5.32±0.01	5.71±0.01	5.21±0.1	6.68±0.15*
	3	4.23±0.13*	4.96±0.05	5.32±0.07	4.71±0.21
The relative volume of the colloid, %	1	20.56±1.07	20.74±0.92	24.73±2.52	28.92±1.52
	2	7.03±1.6*	11.48±0.73	8.84±1.61	9.82±1.75
Relative volume of the follicular epithelium, %	1	23.93±2.1	22.84±0.62	17.87±1.05	23.25±1.27
	2	30.42±1.79	25.48±0.54	24.78±1.15	26.9±1.75
Relative volume of the interfollicular epithelium, %	1	15.44±1.61	11.18±1.02	13.47±2.58	11.72±0.23
	2	15.51±1.04	13.85±0.45	18.9±2.03	20.93±1.52
Relative stroma volume, %	1	17.72±1.73	23.99±2.03	21.14±1.08	19.05±1.93
	2	27.44±1.86	26.05±2.5	23.81±1.64	20.07±1.79
	3	26.42±2.6	26.28±1.77	28.51±1.9	22.27±1.05
Relative volume of the vascular bed, %	1	19.08±3.05	16.4± 1.73	17.01±2.9	13.5±1.81*
	2	19±1.94	15.64±1.68*	18.27±2.03	19.61±2.5
	3	19.63±3.4	20.3±1.75	17.02±1.2	20.73±2.06

Note: Morphofunctional types: 1 – follicular-colloidal type; 2 – mixed type; 3-desquamative type.
* – $p < 0.05$ when comparing the age groups within each type.

With an increase in gestation timing, children of both nationalities experienced an increase in sclerosis index, which probably indicated gland rearrangement from stromal to parenchymal variant. But the Yakuts had this indicator throughout the gestational period lower than the Russians.

When analyzing morphometric indicators, depending on nationality and sex, reliable differences were found between Yakut boys and Russian boys in the following parameters: the relative volume of follicular epithelium was significantly higher in Russian boys 31.68 + 0.8 % than in Yakuts 28.4 + 1.15 % ($p < 0.05$). Indicators of the relative volume of the vascular channel in Yakut boys were 20.28 + 0.67 % higher ($p < 0.05$) than in Russian 17.85 + 0.61 %. The sclerosing index was significantly ($p < 0.001$) higher in Russian boys 2.01 + 0.05 than in Yakut boys 1.67 + 0.06. The blood supply index, also, was higher in Russian boys 1.37 + 0.04 than in Yakuts 1.22 + 0.04 ($p < 0.05$). The same trend was observed between Yakut girls and girls of Russian nationality as in boys, but no statistically significant differences were found.

Thus, stromal structural components of the thyroid gland were expressed in fetuses and newborns of Yakut nationality and children of Russian nationality, on the contrary, had more structural components of parenchyma.

4. CONCLUSIONS

High rates of the desquamative type of gland indicating functional tension of this organ, as well as high rates of thyroid thyroid volume in fetuses and newborns in Yakutia, when compared with similar data for the non-edemic region of St. Petersburg, are probably associated with iodine insufficiency of the Republic of Sakha (Yakutia).

The height of the lobes was lower, and the thickness and width of both lobes were higher in fetuses and newborns of indigenous nationality, at all gestation periods, ($p < 0.05$) than in non-indigenous.

Thus, fetal gland differed in national characteristics in fetuses and newborns. This was probably due to the anthropometric features of the indigenous inhabitants of the Republic of Sakha (Yakutia): a relatively low height, a short neck.

Stromal structural components of the thyroid gland were more pronounced in fetuses and newborns of Yakut nationality. Children of Russian nationality, on the contrary, had more structural components of the parenchyma. Perhaps this phenomenon was due to genetic factors. For example, some researchers had confirmed the role of genetic factors modulating the risk of thyroid disease [4, 7, 8]. When analyzing the incidence of allelic variants in genes, in autoimmune thyroid diseases, significant inter-ethnic differences were found [7, 8].

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