Study of the functional state of the thyroid gland in pregnant women with hypothyroidism

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Abstract. Currently, hypothyroidism is emerging as a significant issue worldwide. According to statistics, the global incidence of hypothyroidism is second only to diabetes. Various types of iodine deficiency diseases are recognized, including hypothyroidism, endemic goiter, hyperthyroidism, thyroid cancer, etc. The prevalence of hypothyroidism ranks first in Kazakhstan. Changes in the level of thyroid hormones during the reproductive period can also significantly impact the expectant mother and the developing fetus. Many chemicals that pollute the environment inhibit protective immunophysiological mechanisms, reduce the body's ability to adapt, increase the frequency of reproductive system diseases, and alter their course. A decrease in the quality of the environment, social discomfort, and large man-made disasters lead to environmentally dependent transitions and pathological changes in various organs and systems of a person, resulting in a decrease in life expectancy. In this regard, improving the health of the population is an important issue in medicine. In this article, a comparative analysis of the development of hypothyroidism in pregnant women in Almaty and Aktobe was carried out.

1 Introduction

In our country, hypothyroidism is a pressing health problem. According to the World Health Organization, Kazakhstan has a high incidence of hypothyroidism. The main causes of hypothyroidism, in general, are iodine deficiency in food and water [1], as well as a low level of medical awareness in the population.

The prevalence of hypothyroidism during pregnancy is relatively higher in Asian countries than in Western countries, with geographical variability ranging from 2.5 to 11% [2].

Research published in recent years on the perinatal consequences of maternal thyroid dysfunction during pregnancy has led to a growing debate about the need to develop strategies for universal or selective screening for these changes in pregnant women [3].

The main etiology of hypothyroidism during pregnancy is iodine deficiency. And in iodine-sufficient countries, the main cause is autoimmune thyroiditis. Pregnant women with hypothyroidism include fatigue, anxiety, constipation, muscle cramps, and weight gain [4-6]. Maintaining euthyroidism in a pregnant mother is important for healthy fetal growth and

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development. Even minor changes in the functioning of the mother's thyroid gland can have a detrimental effect on the fetus, in addition to possible adverse effects on the pregnancy itself [7].

The thyroid-stimulating hormone (TSH) is a sensitive marker of thyroid dysfunction. However, physiological changes during pregnancy require specific circulating stimulating hormone and free thyroxine ranges to properly assess the function of the mother's thyroid gland [8].

Many scientists have conducted studies on hypothyroidism [9-12], with one study recommending regular screening of thyroid function in the first trimester of pregnancy, as it provides an effective way to detect gestational thyroid dysfunction [13].

There is a certain association between the development of endemic goiter and the increase of technical xenobiotics in the environment. Goiter endemism with a high technogenic load has its characteristics: a high prevalence of goiter, a clear frequency of autoimmune thyroiditis and nodular goiter, and subclinical and clinical hypothyroidism [14].

Thyroid hormones affect metabolic processes, one of which is the caloric effect of thyroid hormones, causing tissues and organs to consume more oxygen. Tissues and organs respond in different ways to the caloric effect. When carrying out thyroid hormone therapy in patients with hypothyroidism, it should be borne in mind that there is a high sensitivity of the myocardium. The hormones T3, and T4 (total and free T4) also regulate cholesterol metabolism, increasing its degradation and bile excretion. Therefore, with hypothyroidism, the level of cholesterol in the blood increases. [15].

Deterioration of environmental conditions and the effect of various emissions on the function of the thyroid gland is one of the causes of secondary iodine deficiency. In the Western region of Kazakhstan, an anthropogenic province has been formed due to the contamination of soil and water with chromium, boron, and fluorine.

The norm of the TSH level in the blood depends on many factors, including age, gender, physical activity, time of day, and even the time of year [l6].

The purpose of our study is to compare the indicators of pregnant women with hypothyroidism in two cities of Kazakhstan: Almaty and Aktobe.

Validation of the study was affected by the location and ecological conditions of cities. Aktobe is located in the northwestern part of Kazakhstan, and its ecological situation differs from that of Almaty. Air pollution in Aktobe is primarily associated with industry, as the city serves as a major center for the oil and gas industry. This can lead to pollution of air and water resources [17, 18].

2 Materials and Methods

2.1 Participants

The study involved 20 pregnant women (with an average gestational age of 16 weeks) aged 28-35 years who provided written consent (three groups: healthy control (group 1 - 4 pregnant women from Almaty, 4 from Aktobe) and two hypothyroid groups from Almaty (group 2, n=6) and Aktobe (group 3, n=6). Hypothyroid pregnant women took medications as prescribed by the doctor throughout the entire period of pregnancy.

2.2 Biomarkers of thyroid function

In addition to a general blood examination, hormone results (T3, T4, TSH) indicating the functioning of the thyroid gland were evaluated. TSH was measured using free T4 ECLIA

technology [18]. The research was conducted on women registered in the Invivo laboratory center of the clinics of Almaty and Aktobe from August 2022 to March 2023.

2.3 Statistical Analysis

The data was reported as the means ± SD. The significance of the differences between the means of groups was assessed by unpaired two-tailed Student's t-test. $p<0.05$ was considered statistically significant. Statistical analysis was performed with the GraphPad Prism 6.0 Program (GraphPad Software, San Diego, CA).

3 Results and Discussion

According to the Ministry of Health of the Republic of Kazakhstan, the incidence of hypothyroidism in pregnant women is higher. In some regions of Kazakhstan, the proportion of pregnant women with hypothyroidism reaches 10-15%. In our study, pregnant women living in Almaty and Aktobe were included.

In adults, total T3 in a blood test is detected at a concentration of 0.90-2.80 nmol/l; in pregnant women, its level increases to 1.70-3.0 nmol/l. Free T3 is normally 3.1–6.8 pmol/l.

In the I trimester in all groups and types of hypothyroidism, the main indicator of the normal state of the total hormone T3 in group control was 1.87±0.09 nmol/l, and free T3 was 4.35±0.21pmol/l. In hypothyroidism, total T3 was 0.96±0.04 nmol/l in the city of Almaty, and 0.71±0.03 nmol/l in the city of Aktobe. The free T3 indicator was 2.9±0.14 pmol/l in Almaty city and 2.1±0.10 pmol/l in Aktobe city. Total and free T3 values were lower than normal in the experimental groups.

In II trimesters, the main indicator of the normal state of total T3 was 2.35±0.11 nmol/l, and free hormone T3 in hypothyroidism was 5.25±0.26 pmol/l. The total T3 level in Almaty was 1.71±0.08 nmol/l, and in Aktobe, it was 1.4±0.07 nmol/l. The free T3 indicator was 4.5±0.22 pmol/l in Almaty and 3±0.15 pmol/l in Aktobe.

The normal in hypothyroidism during the III trimester range for total T3 is 2.67±0.13 nmol/l and free T3 levels are 5.8±0.29 pmol/l. The general T3 level in Almaty was 1.81±0.09 nmol/l; in Aktobe, this indicator was 1.53±0.07 nmol/l. The free level of T3 in Almaty was 4.5±0.22 pmol/l and Aktobe ranged from 2.6±0.13 pmol/l (table 1).

Table 1. Indicators of total and free T3 hormone in hypothyroidism of pregnant women in the I, II, and III trimesters.

Trimester	Groups	T3 total, nmol/l	T3 free, pmol/l
I trimester	Control	1.87±0.09	4.35±0.21
	Almaty	0.96±0.04*	2.9±0.14*
	Aktobe	0.71±0.03*	2.1±0.10*
II trimester	Control	2.35±0.11	5.25±0.26
	Almaty	1.71±0.08*	1.4±0.07*
	Aktobe	4.5±0.22*	3±0.15*
III trimester	Control	2.67±0.13	5.8±0.29
	Almaty	1.81±0.09*	4.5±0.22*
	Aktobe	1.53±0.07*	2.6±0.13*

Note: *p-value < 0.05.

Statistical analysis revealed that hypothyroid pregnant women even treated with hormones have significantly less ($p<0.05$) plasma level T3 both total and free. It is impossible to diagnose a subclinical form of hypothyroidism by the concentration of thyroid hormones,

as their levels are within physiological norms and there are no symptoms of the disease. However, latent-type hypothyroidism can be suspected if there is a slight increase in the level of TSH or if its concentration changes at the upper limit of normal indicators. Subclinical hypothyroidism should not be ignored. With this condition, a person may not initially complain about the symptoms of the disease, and then it begins to progress rapidly.

In patients with moderate hypothyroidism, the diagnosis is more pronounced. It was established based on decreased free and total T4 levels in the blood below normal. Our research shows the total and free indicators of the T4 hormone in pregnant women with moderate hypothyroidism in Almaty and Aktobe in the following table (table 2).

The level of free thyroxine in the blood is measured in picomoles per liter (pmol/l) and a concentration of 10.3-24.5 pmol/l is considered normal, and the concentration of total T4 is in the range of 66.9-160.9 nmol/l. T4 total was stable at 82.5±4.12 nmol/l in the I trimester, 136.5±6.82 nmol/l in the II trimester, and 158.5±7.92 nmol/l in the III trimester in the control groups in general normal condition. Experimental groups II and III decreased in indicators in every trimester.

Total T4 in the first trimester in the Almaty group was 26.4±1.32 nmol/l, in the Aktobe group 24.7±1.23 nmol/l; second trimester in the Almaty group 28.5±1.42 nmol/l and Aktobe group 26±1.31 nmol/l; the third trimester is slightly higher than the other semesters, but despite this it is lower than the norm, Almaty group 31.4±1.57 nmol/l and Aktobe group 30.8±1.54 nmol/l.

Free T4 showed normal values in the first groups in each trimester under normal conditions; the first trimester in the Almaty group was 7±0.35 pmol/l and Aktobe group 6±0.3 pmol/l; the second trimester in the IInd group 5.9±0.29 pmol/l and Aktobe group 5.2±0.26 pmol/l; the third-trimester Almaty group 5.6±0.28 pmol/l and Aktobe group 4.8±0.24 pmol/l.

Table 2. The concentration of T4 total and T4 free hormones in pregnant women with hypothyroidism during the I, II, and III trimesters

Trimester	Groups	T4 total, nmol/l	T4 free, pmol/l
I trimester	Control	82.5±4.12	24.5±1.22
	Almaty	26.4±1.32*	7±0.35*
	Aktobe	24.7±1.23*	6±0.3*
II trimester	Control	136.5±6.82	21±1.05
	Almaty	28.5±1.42*	5.9±0.29*
	Aktobe	26±1.31*	5.2±0.26*
III trimester	Control	158.5±7.92	20.4±1.02
	Almaty	31.4±1.57*	5.6±0.28*
	Aktobe	30.8±1.54*	4.8±0.24*

Note: *p-value < 0.05.

The default TSH values should be in the first trimester 0.1–2.5 mIU/L, in the second trimester 0.2–3.0 mIU/L, and in the third trimester 0.3–3.5 mIU/L. According to our study, in Almaty, compared with Aktobe, the indicators of mild hypothyroidism of the hormone TSH in pregnant women prevailed. The incidence of hypothyroidism increased from 8.1±0.40 mIU/L to 14.7±0.73 mIU/L in the third trimester compared to the first trimester. This means that in Almaty there are many pregnant women with mild hypothyroidism, and it can be concluded that their number increases with the duration of pregnancy (table 3).

Table 3. The concentration of TSH hormones in pregnant women with hypothyroidism during the I, II, and III trimesters

Trimester	Groups	TSH, mIU/L
II trimester	Control	1.3±0.06
	Almaty	8.1±0.40*

	Aktobe	7.2±0.36*
II trimester	Control	1.6±0.08
	Almaty	10.2±0.51*
	Aktobe	9±0.45*
III trimester	Control	1.4±0.07
	Almaty	14.7±0.73*
	Aktobe	13.5±0.67*

Note: *p-value < 0.05.

In our experience, the relative value of the TSH hormone in the three types of hypothyroidism of pregnant women in the I, II, and III trimesters was several times higher than the normal value. TSH hormone plays a crucial role in diagnosing hypothyroidism in pregnant women because in some cases T3 and T4 hormones remain unchanged. Summarizing the indicators of total T3 and free T3 hormone, it can be observed that the indicator of T3 in moderate hypothyroidism of pregnant women is lower than normal. And, based on the results of total T4 and free T4 hormones, we compared the values of pregnant women with mild and moderate hypothyroidism. In these two cases, it is seen that the level of T4 hormones is several times lower than the normal level. In subclinical hypothyroidism, we can see that T3 and T4 hormones are in normal condition or lower than normal, and at the same time, the TSH hormone is raised from normal level to high value.

By the concentration of thyroid hormones, it is impossible to determine the mild form of hypothyroidism, as well as the subclinical form, since their level is at the lower limit of physiological norms. However, mild hypothyroidism may be suspected in patients with eliminated symptomatology and an increase in serum TSH levels up to 20 mm/l. Thus, it indicates the severity of thyroid dysfunction in the milder form of hypothyroidism compared to subclinical hypothyroidism.

4 Conclusion

TSH level in pregnant women in Almaty is higher than in other regions, influenced by various factors, including environmental conditions, the quality of drinking water, and nutrition, as well as hereditary factors. When analyzing the prevalence of hypothyroidism in individual cities, Aktobe showed a low prevalence of hypothyroidism (8%), with the highest indicator found in the city of Almaty (mountainous region) (13.2%) from August 2022 to March 2023. Analyzing the functional state of the thyroid gland in women with reproductive dysfunction, it can be noted that the function of the reproductive system is determined by the harmonious functioning of the complex neuroendocrine interaction. Therefore, timely diagnosis and prediction of possible and correction of identified complications of hypothyroidism in pregnant women are the main ways to achieve a successful outcome of pregnancy and childbirth for the mother and fetus.

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