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Research Article

Laboratory Diagnostics of Thyroid Disorders

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ABSTRACT.

Nowadays, thyroid disorders are one of the most widespread diseases in the world. Among endocrine diseases they occupy the second place after diabetes mellitus. In thyroid endemic areas thyroid disorders are met in 38.9% of adults and 53.3% of children [29,30]. Taking into account that Kabardino-Balkar Republic (KBR) is a region with natural iodine deficiency, the problem appears very acute. The purpose of the study is to evaluate basal level of thyroid hormones in patient blood serum and identification of laboratory parameters at different age groups diagnostics.
Materials and Methods.The analysis of the laboratory data of 261 patient aged 21 – 80, who were examined in "State Clinical Hospital №1" in Nalchik city, was performed. The results of the study showed that out of 173 examined

women, 68 had high hormones levels, 60 patients had normal levels and 45 had low levels. High hormones levels were observed in 39 men, normal levels in 18 and low levels in 31 patients.

Key words: thyroid stimulating hormone (TSH), iodine deficiency conditions, hypothyroidism, diagnostics, enzyme-linked immunoassay (ELISA).

INTRODUCTION

Thyroid gland (TG) is the biggest endocrine gland in human body. Average TG weight in an adult human is 18–20 g. Thyroid is enclosed in a fibrous capsule and is attached to the anterior and lateral larynx sides by a layer of loose connective tissue. Two thyroid lobes lie on both sides of larynx and trachea and are connected with each other by a thin tissue stripe called isthmus.

Thyroid tissue is filled primarily with spherical thyroid follicles. Each follicle consists of a layer of cuboidal cells (thyrocytes) that surround a cavity filled with colloid that primarily containsthyroglobulin (TG). The cells apical surface is inward oriented, they have microvilli that penetrate into the colloid. Interfolicular space is well fed by blood capillaries.

Thyroglobulin (TG) is the initial substrate for thyroxin (T4) and triiodothyronine (T3) synthesis. T4 and T3 regulation and synthesis is exerted bythyroid stimulating hormone (TSH) produced by pituitary gland.

Hypothyroidism is a clinical syndrome that is associated with a persistent decrease of thyroid hormones levels in the organism. This syndrome was first described in 1873 by V. Gall. There are age and sex specific differences in the hypothyroidism epidemiology [1,2]. Nearly all the published epidemiologic studies indicate on the age-related increase of hypothyroidism rate. Primarily, this is associated with the fact that it is mainly caused by Hashimoto's thyroiditis – a destruction of thyroid gland [3].

Hypothyroidism is classified as primary, secondary and tertiary. Primary hypothyroidism develops at thyroid disorders and is associated with thyroid stimulating hormone (TSH) level increase.

Secondary hypothyroidism develops at pituitary-hypothalamic system disorders and is associated with insufficient production of TSH and further decrease of thyroid functioning [4].

Tertiary hypothyroidism develops at hypothalamus disorders.

As a rule, clinical picture is not clear and TG disorders are disguised by other diseases symptoms. Some patients can have prevailing neurological symptoms, while in others main clinical symptom of thyroid pathology can bearterial hypertension or retrosternal pains. Sometimes, main symptoms can be gastrointestinal tract disorders like nausea, meteorism or constipation [5,6,7].The most severe iodine deficiency disorder is cretinism, which is an incurable pathology. It is characterized by severe mental retardation, dwarfism, skeletal deformation and deaf-dumbness. Cretinism can have a neurological or mixed ematous form. The first one is associated with the lack of thyroid hormones during the critical period of fetus development in the beginning of the III trimester of pregnancy. Myxedematous form is considered to result from chronical hypothyroidism during the later stages of prenatal development and earlier stages of postnatal life [8,9,10]. In elderly people at long-term thyroid tissue iodine deficiency, nodules are formed that secrete thyroid hormones in autonomic mode, i.e. independently from TSH. Hence, goiteror toxic thyroid multinodule develops. In many cases,thyrotoxicosis is induced by acute increase of iodine availability coming with food products with high iodine content or with iodine containing drugs or diagnostic agents [11, 12].

TSH secretion is regulated bycircadian rhythms with an acrophase at night time. The highest concentration of TSH in blood is observed by 2 – 4 am, high levels of TSH in blood are also

identified at 6 – 8 am, minimal values of TSH are observed at 7 – 6 pm.

Normal secretion rhythm is disturbed at wakefulness at night time. With aging the concentration of TSH slightly increases and the amount of secreted hormone at night time decreases [9, 13, 14].

TSH secretion is inhibited during standard therapy or during postsurgical hormone replacement therapy. Increased or decreased TSH levels indicate on inadequate share of the indicated drug, incorrect therapy or presence of antibodies to thyroid antigens. During hormone replacement therapy at hypothyroidism the optimal level of TSH lies within lower threshold range of the reference [15, 16].

The concentration of TSH in blood can also decrease because of indication of anabolic steroids, corticosteroids, cytostatics, β-adrenomimetics (dobutamine, dopexamine), dopamine, amiodarone (hyperthyroid patients),thyroxin, triiodothyronine, carbamazepine, somatostatin and octreotide, nifedipine and antihyperprolactinemia drugs (metergoline, piribedil,bromocriptine) [17, 18].

During the first part of pregnancy the level of TSH can transiently decreased approximately in 20% of women. In most cases moderate decrease of TSH concentration up to 0.1–0.4 mIU/L is observed. However, in some cases, especially duringmultiple pregnancy, the synthesis of TSH can be totally inhibited. The lowest levels of TSH are observed during 10 – 12th week of pregnancy. In single cases concentration of TSH can remain decreased until lower term of pregnancy [19,20,21, 23].

The majority of iodine in human organism is contained in the form ofthyroxin (T4, L-thyroxin). The main share of T4 (99.97%) circulates in plasma protein bound state. Thyroxin concentration in blood serum is the most common parameter of TG functioning that allows the specialists to differentiate clearly hyper-, hypo- and euthyroidism. Quantitative estimation of free thyroxin is a more reliable parameter for evaluation of TG status than estimation of total triiodothyronine [24, 25, 26].

It is determined that around 10% of patients with clinical symptoms of hypothyroidism have normal level of triiodothyronine (3,3′,5-triiodothyronine, T3). During identification of T3 level in blood serum, it is necessary to take into account its concentration change after exogenous thyroid hormones administration. T3 concentration increase in blood serum is observed during administration of estrogens,heroin, methadone and oral contraceptives. T3 concentration decrease in blood serum is observed during administration of androgens, danazol,dexamethasone, propranolol (at hyperthyroidism), coumarine derivatives and salicylates. T3 biological half-life period is 24 hours [26, 27].

It is well known that presently the main test in laboratory evaluation of the thyroid functional status is TSH level analysis in blood serum. The increase of TSH level in blood is an early sign of not only evident, but also of threatening thyroid insufficiency. TSH level evaluation, along with free T4 and free T3, is one of the main markers during identification of thyroid hormone status. TSH level, in particular, its decrease or complete absence, is considered to be the most sensitive marker at primary hypothyroidism [28].

TSH is a glycoprotein that is produced by anterior pituitary gland. It primarily influences on the thyroid, stimulating thyroxin (T4) and triiodothyronine (T3) synthesis and their expression into blood. Evaluation of TSH concentration in serum is used during the diagnostics of thyroid hyper- and hypofunction, as well as in hormone treatment monitoring during thyroid disorders therapy. TSH is the most sensitive parameter in the diagnostics of thyroid primary pathology.

TSH evaluation before and after thyroid stimulating hormone administration is a more sensitive test than other parameters in hyper- or hypothyroidism diagnostics.

Nowadays, thyroid disorders are one of the most widespread diseases in the world. Among

endocrine disorders they occupy the 2nd place after diabetes mellitus. In thyroid endemic areas, thyroid disorders are diagnosed in 38.9% of adults and 53.3% of children [29, 30].

Taking into account that KBR is a region with natural iodine insufficiency, it can be concluded that this problem is very acute in the Republic. It is found that KRB biocenosis has a complex of natural and anthropogenic factors that obligatory influence on the development of thyroid disorders. The most significant among them are iodine deficiency and lack of iodine deficiency preventive measures, insolation and radioinduced diseases, different climate zones related stress and anthropogenies with disruptors of age and sex specific disproportion [31,32].

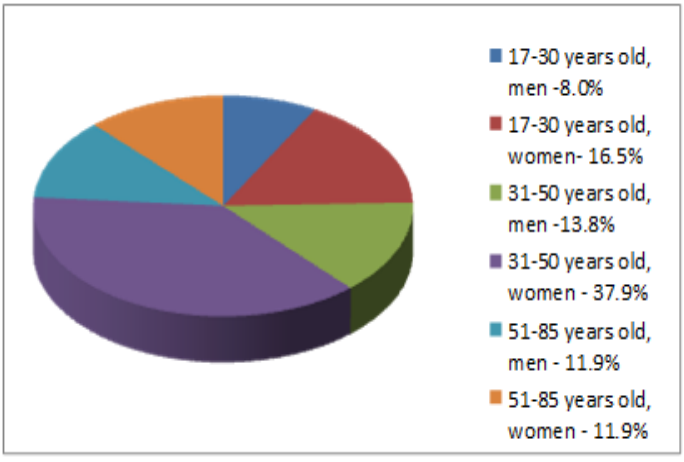
The purpose of the study was to evaluate basal levels of thyroid hormones in patient blood serum and to analyze laboratory parameters during hypothyroidism diagnostics in different age groups.

MATERIALS AND METHODS.

The analysis of the laboratory data of 261 patient aged 21 – 80, who were examined in "State Clinical Hospital №1" in Nalchik city, was performed. The study enrolled 173 women (66.3%) and 88 men (33.7%).

The distribution of the examined patients by age and sex is presented in the Diagram 1.

Diagram 1: Distribution of patients with hypothyroidism by age and gender.



The patients had their levels of TSH, free T4 and free T3 in blood identified by ELISA analysis. The researchers used fresh blood serum samples taken after fasting for the analysis.

Laboratory parameters were identified by reagents kit «Diagnostics systems» on BIO-RAD analyzer.

Blood sampling was performed according to the principles of aseptics. After blood clutter formation, the serum was separated by centrifuging.

Quantitative assay of hormones by the method of solid phase ELISA is a complicated procedure, which has to be performed only by highly qualified specialists. One of the main factors in precise hormone evaluation in blood samples is preanalytical analysis stage, which includes proper blood sampling in the examined patient and proper blood sample preparation for laboratory assay [24,33,34,]. During quantitative assay of hormones in laboratory it is important to remember that hormone concentration can increase after meal; hormone concentration in blood is regulated by circadian rhythms; a number of drugs influence on the concentration of the tested hormones in blood, increasing or decreasing their level; hormones concentration can change by 10% and more depending on the vertical or horizontal patient body position during blood sampling, as well as preceding physical activity. The hormone level evaluation is also influenced by blood hemolysis, which can develop during long-term venostasis, active aspiration of blood by a syringe and high or low temperature exposure on blood after sampling [35, 36, 37, 38, 39].

RESULTS AND DISCUSSION.

Hormone system is one of the main systems that regulates metabolism and maintains homeostasis. It integrates the functions of all the endocrine glands that express hormones directly into the circulating blood.

Modern clinical biochemistry methods facilitate qualified and well-founded diagnostics, adequate treatment indication and evaluation of prognosis at numerous hormonal disorders.

Clinical biochemical assays are primarily used to confirm or specify the diagnosis, characteristics of the form and severity, disease outcome prognosis, to select etiologic and pathogenetic therapy.

Depending on the clinical tasks, biochemical assays can be performed once or repeatedly (in dynamics). Hormones concentration in blood and tissues is very low, so it is necessary to use highly sensitive methods of evaluation.

Hormone concentration evaluation results, obtained in different laboratories by different diagnostics kits, can vary significantly. Hence, during the assay it is necessary to compare the obtained results with the normal diagnostic values, specified for the used test system because they can express results in different units of measurement.

For diagnostics of functional activity of thyroid it is recommended to use diagnostic kits of the full range of thyroid hormones, manufactured by one company [33, 35, 40, 41, 42, 43,].

Improvement of iodine deficiency diagnostic methods will allow the researchers to develop new economically beneficial methods and medical approaches to the prevention and treatment of thyroid disorders in regions with low level of iodine consumption and at thyroid pathologic condition in people who live in the region with mild iodine deficiency (Nalchik). The authors of the study identified the levels of TSH, free T4 and free T3 in patients blood serum by the ELISA method to evaluate the diagnostic and prognostic values of these parameters.

Enzyme-linked immunoassay (ELISA) is used for levels identification of thyroid hormones and a number of high molecular compounds that influence on the thyroid function. ELISA method allows the researches to obtain important information on preclinical pathology development and, due to this, significantly improve the therapy efficiency.

Nowadays, ELISA methods are considered to be the main ones for identification of thyroid function disorders, for differentiated diagnostics and for treatment monitoring.

The results of the present study are shown in Tables 3 and 3.

Out of 173 examined women, high hormone levels were observed in 68 patients, normal levels – in 60 patients and low levels – in 45 patients.

High levels of hormones were observed in 39 men, normal levels – in 18 patients and low levels – in 31 patients.

According to the Table 2, TSH levels in blood serum were from 0.11 to 45.6 uIU/mL; free T4 levels were from 4.3 to 36.8 pmol/L; free T3 levels were from 0.48-13.7 uIU/mL.

Table 2: Gender dependent mean hormone levels in blood serum of the examined patients.

Group	Hormone levels in patients blood serum					
	TSH	Reference values	Free T4	Reference values	Free T3	Reference values
Men	0.15-25.9	0.4-4.0 uIU/mL	5.0-30.1	9.0-22.2 pmol/L	0.55-12.6	2.5-7.5 pmol/L
Women	0.11- 45.6	0.4-4.0 uIU/mL	4.3-36.8	9.0-22.2 pmol/L	0.48-13.7	2.5-7.5 pmol/L

In women aged 31 – 50 high levels of hormones were observed, TSH up to 45.6 uIU/mL, free T4 up to 36.8 pmol/L, free T3 up to 13.7 pmol/L (Table 3).

High levels of THS were identified in men born in 1984 – 1997 and were in the range from 0.17 to 25.9 units. The tendency towards higher values of this parameter was observed in women in comparison with men (Table 3).

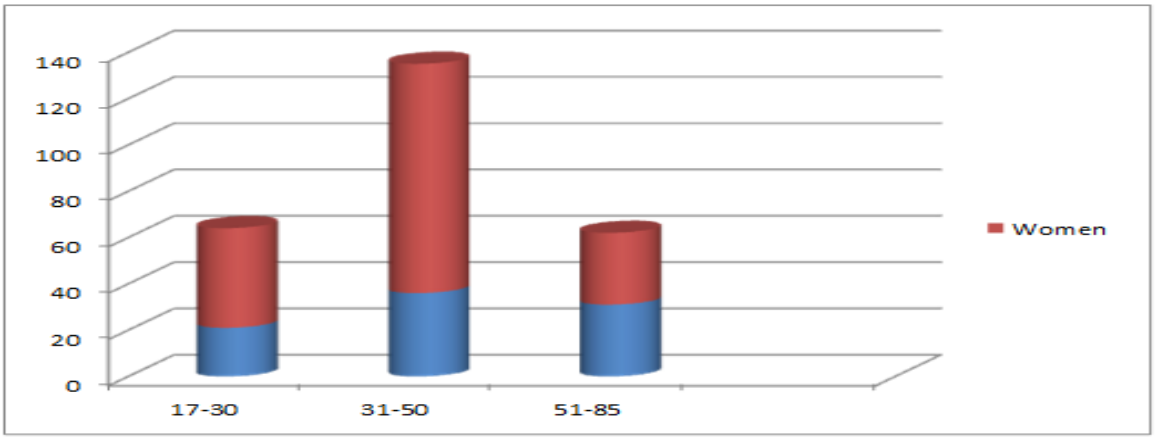
Mean levels of TSH in the tested groups, as well as mean levels of free T4 and free T3, were higher among the examined women (Table 3).

Table 3: Mean hormone levels in blood serum in the examined patient groups aged from 17 to 85.

Group	Age	Hormone levels in blood serum		
		TSH, uIU/mL	T4 free, pmol/L	T3 free, pmol/L
Men	17-30 years old	0.17– 25.9	5.8– 28.5	0.88– 10.4
	31-50 years old	0.15– 20.4	5.0– 30.1	0.55– 12.6
	51-85 years old	0.22– 12.0	5.6– 27.9	0.99 – 9.5
Women	17-30 years old	0.17– 37.2	4.9– 29.6	0.56– 13.5
	31-50 years old	0.11– 45.6	4.3 – 36.8	0.48– 13.7
	51-85 years old	0.20– 12.6	5.7– 28.3	1.01– 10.5

According to the authors' data (Diagram 2), women in the Republic are more prone to hypothyroidism than men, especially at the age of 31-50 years old.

Diagram 2: Mean age-specific ratio of men to women prone to hypothyroidism



The patients aged 30 – 50 represent a high risk group, so early diagnostics of hormonal changes reduces the risk of hypothyroidism development.

Hence, based on the results of the present study and the data obtained by other researchers, it can be concluded that identification of TSH levels, along with free T4 and free T3, is one of the main markers during evaluation of thyroid hormonal status. TSH (in particular, its decrease or complete absence) is the most sensitive marker at primary hypothyroidism.

Identification of TSH levels before and after TSH administration is a more sensitive test than other parameters in diagnostics of hyper- or hypothyroidism.

Mean TSH levels in the tested groups, as well as mean levels of free T4 and free T3, were significantly higher than among the examined women.

Antibodies identification by ELISA test can be used for specification of pathogenesis, as well as for improvement of this disease immunodiagnostics and prognosis of the disease clinical forms.

CONCLUSIONS

1. Mean TSH levels in patients blood serum were from 0.11 to 45.6 uIU/mL; free T4 levels – from 4.3 to 36.8 pmol/L; free T3 levels – from 0.48 to 13.7 pmol/L.
2. Women aged 31 – 50 years old had higher levels of TSH up to 45.6 uIU/mL, free T4 levels up to 36.8 pmol/L, free T3 levels up to 13.7 pmol/L.
3. High levels of TSH were observed in men born in 1984 – 1997 and were in the range from 0.17 to 25.9 units.
4. Mean TSH levels in the tested groups, as well as mean free T4 and free T3 levels, were higher in the examined women.
5. Patients aged 30 – 50 are in the group of high risk, so early diagnostics of hormonal changes significantly reduces the risk of hypothyroidism development.

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