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ULTRASOUND DIAGNOSIS OF MORPHOLOGICAL CHANGES OF THE THYROID GLAND AFTER CORONAVIRUS INFECTION

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The entry of SARS-CoV-2 into the nervous system induces stress, vasodilatation and thrombogenesis by increasing the oxidative effect of the virus, which can lead to pituitary hemorrhagic apoplexy [2].

The authors suggested the possibility of hypophysitis or virus directly affecting the hypothalamus, which could lead to a state of hypothalamic-pituitary dysfunction [3]. L. Wei et al. showed damage to the hypothalamus and pituitary gland, as well as autopsy of the pituitary gland in patients infected with coronavirus. They showed a decrease in the number of somatotropic, thyrotrophic and corticotropic cells in the pituitary gland, and acute damage changes such as swelling and degeneration of neurons. These results were consistent with serological data on the decrease in blood plasma levels of growth hormone, thyroid-stimulating hormone (TSH) and adrenocorticotropic hormone (ACTH) [4].

According to the results of the post-mortem study of patients infected with SARS-CoV-2, pathological changes were detected in various organs, including the thyroid gland [5].

Autopsy results of 5 patients infected with SARS-CoV revealed signs of thyrocyte apoptosis, desquamation of epithelial cells, loss of colloid by follicles without signs of necrosis or lymphocytic infiltration; The authors do not exclude the direct effect of the virus on the thyroid gland [6]. However, Y. Ding and others could not detect the virus or its antigen in thyroid tissue [7].

A study conducted during the SARS-CoV-1 epidemic provided detailed information on thyroid histopathology results from patients with SARS [8]. The results showed that parafollicular cells and follicular epithelial cells were severely damaged; caused the rupture of follicles due to the destruction of epithelial cells. However, no inflammatory infiltration or cell necrosis was observed, supporting the hypothesis that extensive apoptosis causes thyroid damage in SARS-CoV-1 infection. In general, the differences in thyroid morphology data between SARS-CoV-1 and SARS-CoV-2, on the contrary, SARS-CoV-2 may cause a more severe infection, the relative severity of which is higher than that of SARS-CoV-1. Of course, information about the effect of SARS-CoV-1 on the structure of the thyroid gland is still insufficient.

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Compared with normal thyroids, patients infected with SARS-CoV are characterized by follicular cell damage, epithelial destruction, epithelial cell migration, hyperemia of capillaries in the connective tissue between follicular cells, and the development of fibrosis in the connective tissue. However, no inflammatory infiltration or cell necrosis was noted, supporting the hypothesis that extensive apoptosis causes thyroid damage in SARS-CoV [1]. If these morphological changes observed in SARS-CoV infection are also observed in SARS-CoV-2 infection, this may explain the low serum levels of thyroxine (T4) and triiodothyronine (T3) in patients with severe novel coronavirus [4]. In the autopsy of patients who died from SARS-CoV-2, morphological and pathological changes were found in various organs, including the thyroid gland [8].

The study of the histomorphological structure of the thyroid tissue shows that the diffuse form of the disease is mainly characterized by clear atrophic changes in the parenchyma, diffuse sclerotic changes in the stroma, infiltration of lymph-plasma cells and its nodular form, atrophic and sclerotic changes in the epithelium, as well as the presence of an unclear capsule. in the focal form, it is characterized by the presence of various focal infiltrates in the stroma of the gland. Based on the above, it should be noted that the histopathological changes characteristic of autoimmune thyroiditis are not manifested to the same extent in different parts of the thyroid gland. Thus, severe pathological changes detected in one part of the same gland in another area are replaced by relatively milder lesions. In short, histomorphological changes in autoimmune thyroiditis are heterogeneous [9].

Ultrasound diagnosis is a safe and informative method for the diagnosis of endocrine diseases. Analysis of thyroid ultrasound data in healthy and sick people showed that the size of the thyroid gland in patients with euthyroidism, hypothyroidism, hyperthyroidism and diffuse toxic goiter does not have significant differences in gender and age. In women and men, regardless of age, it was observed that the size of the thyroid gland was significantly ($r<0.001$) smaller in hypothyroidism. It is important to note that in patients with euthyroidism, hyperthyroidism, and diffuse toxic goiter, the volume of the thyroid gland is at the level of the upper limit of the physiological norm or exceeds it. And in patients with hypothyroidism, this parameter was lower than the standards accepted in practical health care.

From the point of view of topical diagnostics, it is possible to get more information with radiation diagnostic methods, which are rapidly developing in recent years. [10].

Therefore, almost all modern diagnostic algorithms, domestic and foreign, today include certain instrumental methods, the most popular of which is ultrasound examination [11].

Today, Ultrasound is the "gold standard" for the detection of thyroid nodules all over the world, as well as in Russia [12]. The advantages of this method are recognized all over the world despite subjectivity. The American Thyroid Association recommends that all patients with a known or suspected nodule in the QB should have a thyroid ultrasound. Ultrasound examination can not only see the topical location of the thyroid gland, but also make a differential diagnosis with tumor formations of other etiologies and detect metastases in the lymph nodes [12].

Ultrasound examination of the thyroid gland evaluates its location, structure and size [1]. Many scientists consider the problem of age-related approach in determining its normal dimensions by ultrasound examination of the thyroid gland to be important [6]. It is not only fundamental from the point of view of science, but also of practical importance, because one of the main manifestations of identifying various diseases of the thyroid gland and pathological processes in it is the absolute or relative change in the volume of the entire gland or its parts. But until now, scientists from different countries have not agreed on the criteria for evaluating the ultrasound size of the thyroid gland [2].

There are many ways to determine the size and volume of the thyroid gland [4]. The ultrasound method is one of the modern and common methods of thyroid examination. Blum Manfred (2020) stated that thyroid ultrasound is a useful, safe and cost-effective way to visualize the state of the gland and its pathology [2,4].

The ultrasound method is useful, practical and safe in evaluating the size of the thyroid gland [8]. In the daily practice of a modern doctor, it is very important to study the information about the limits of anatomical variability of the gland in order to further improve the diagnosis process in order to diagnose thyroid gland diseases using ultrasonography, to determine the parts and total volume of the thyroid gland under normal conditions. Local and foreign scientists recognize the existence of specific characteristics of the thyroid gland [2,8].

Information obtained on thyroid volume in Ultrasound is necessary to evaluate a number of pathophysiological factors, such as multinodular goiter, thyroiditis, and thyroid cancer [12].

The annual increase in the incidence of nodular goitre is approximately 0.1% in the young and 2% in the elderly, with a female-to-male ratio of 4:1 [13]. Researches conducted all over the world show that this is not only related to the growth of KB pathology, but also to the improvement of the quality of diagnosis. Currently, everyone can undergo an ultrasound examination of other organs along with the examination of the thyroid gland. This situation, according to statistics, caused that every second inhabitant of the planet is diagnosed with nodular disease of the thyroid gland, or more than 50% of people on the planet have nodules of various sizes [14]. More than 80–90% of people over 70–80 years of age have one or more thyroid nodules, and most of

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these nodules are benign, with a 1–10% risk of carcinoma among all thyroid nodules [15].

According to morphological characteristics, there are nosological forms such as nodular colloid goiter, follicular adenoma, hypertrophic form of autoimmune thyroiditis, solitary cysts, thyroid cancer [3]. According to some studies, with the long-term presence of nodular goiter, only degenerative changes, fibrosis, impaired blood supply, foci of necrosis, cysts and calcifications appear, which, without turning into a cancerous tumor, form the functional autonomy of the thyroid gland due to somatic mutations that lead to the activation of TSH receptors [7].

Today, most of the world's medical institutions use the classification of The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC), which was adopted in 2007 at the conference of the US National Cancer Institute, in the cytological examination of biopts taken from thyroid nodules [15]. Gradually, this system is introduced in Russia as well [4,11]. Most researchers state that the conclusion of a cytologist in TBSRTC should fall into one of 6 categories based on the formula, and this, in turn, requires the cytologist to be in clear and understandable terms for a physician of any narrow specialty [2]. Evaluation of the performance of TBSRTC showed a high degree of correlation between cytological and histological studies and a good predictive ability of cytological examinations for malignant nodules, with a specificity of 93%[11].

The introduction of TIRADS - Thyroid Imaging Reporting and Data System in the primary care setting allowed sonographers to base the guidelines for performing IIPB on thyroid nodules [15].

TBSRTC - The Bethesda System for Reporting Thyroid Cytopathology. It created effective conditions for cytologists to work more effectively in the practice of cytological laboratories [10]. The task of Ultrasound doctors and cytologists is one of the important steps in the process of diagnosis and treatment of thyroid nodules, which is to make a decision on choosing the next stage of treatment [13]. But the initial, main and final point of the diagnostic chain are endocrinological polyclinics [8].

It should also be remembered that several experts inspect the same object and give different, sometimes contradictory, conclusions. This often happens in the subjective assessment of ultrasound and cytological examination images. One of the solutions to the increasing amount of information is the use of expert systems and system analysis methods [5].

The use of such systems [1,3] as an aid or advice in the diagnosis of thyroid diseases allows to achieve accurate results, to use a large amount of accumulated knowledge, and to improve the skills of medical personnel. Characteristics of expert systems [3,7] productivity (making decisions in a short time, in real time), the ability to fill the knowledge base (accumulating practical experience in solving problems) [9], high ease of understanding (authenticity of the proposed solution), generally understandable provides facilities such as language communication [13].

Materials and Methods.

In the study, a total of 116 patients were evaluated for dynamic Ultrasound and hormonal status. The main group was made up of 86 patients with pathology of the thyroid gland function who were infected with SARS-CoV-2, and the control group was made up of 30 relatively healthy people who did not have coronavirus infection.

All patients underwent cervical ultrasound examination according to a standard protocol. Ultrasound examination of the thyroid gland of the subjects involved in the study was carried out in the private clinic "Nazira Med Shifo" in Bukhara using the ultrasound diagnostic scanner MINDRAY DCN60 (made in China) with a convex and linear sensor transducer with a frequency of 7.0-7.5 Hz, standard and new technological methods. done with The study was conducted in ED and TsDK in gray scale mode. The analysis of the obtained results was carried out using the MS Excell program.

Results.

The results of thyroid ultrasound examination of patients in the main and control groups were analyzed. The inspection results were analyzed according to the indicators in Table 1. A comparison of the indicators of ultrasound examination of the thyroid gland in patients of the main and comparative groups showed (Table 10) differences in some of the compared characteristics. Thus, in patients of the main group, the number of cases of average density of the right lobe of the thyroid gland predominated ($\chi2=4.75$; $P<0.05$), in comparison with the indicators of patients in the comparison group. Those examined from the comparison group were characterized by a high density of the right lobe of the thyroid gland ($\chi2=5.34$; $P<0.05$), the presence of smooth contours of the left lobe ($\chi2=41.61$; $P<0.001$), and a predominance of the number of TIRADS-2 ($\chi2=4.85$; $P<0.05$), as well as hypovascularization ($\chi2=4.42$; $P<0.05$).

Table 1. Comparative results of thyroid Ultrasound symptoms of patients in the main and control groups.

Sign		Main group (n=86),%	Control group (n=30), %	χ2	P	OR	Lower. gr. 95% CI	Upper gr. 95% CI
Echo structure of the right lobe	Heterogeneous	86,0	93,3	1,11	0,291	0,44	0,09	2,09
	Homogeneous	14,0	6,7	1,11	0,291	2,27	0,48	10,79
Echo structure of the left lobe	Heterogeneous	84,9	93,3	1,41	0,235	0,40	0,09	1,89

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	Homogeneous	15,1	6,7	1,41	0,235	2,49	0,53	11,76
Echo density of the right lobe	High	9,3	16,7	1,21	0,271	0,51	0,15	1,71
	Average	79,1	83,3	0,25	0,614	0,76	0,25	2,25
	low	11,6	0,0	3,82	0,051	-	-	-
Echo density of the left lobe	High	8,1	10,0	0,10	0,755	0,80	0,19	3,30
	Average	81,4	90,0	1,20	0,273	0,49	0,13	1,80
	low	10,5	0,0	3,40	0,065	-	-	-
Contours of the right lobe	Uneven	26,7	16,7	1,23	0,267	1,83	0,62	5,33
	Smooth	73,3	83,3	1,23	0,267	0,55	0,19	1,60
Contours of the left lobe	Uneven	19,8	10,0	1,49	0,223	2,22	0,60	8,18
	Smooth	22,1	90,0	42,86	0,001	0,03	0,01	0,12
Regional lymph nodes of the right lobe	not enlarged	95,3	90,0	1,12	0,289	2,28	0,48	10,83
	Increased	4,7	10,0	1,12	0,289	0,44	0,09	2,09
Regional lymph nodes of the left lobe	not enlarged	68,6	80,0	1,42	0,234	0,55	0,20	1,49
	Increased	31,4	20,0	1,42	0,234	1,83	0,67	5,00
Structure changes	Heterogeneity	17,4	0,0	6,01	0,014	-	-	-
	anexogenous	1,2	6,7	2,67	0,102	0,16	0,01	1,89
	hypoechoic planes	58,1	16,7	15,34	0,001	6,94	2,43	19,87
	hardened	11,6	26,7	3,84	0,050	0,36	0,13	1,03

	Hyperechoic	5,8	20,0	5,21	0,022	0,25	0,07	0,88
	nodule of cystic consistency	3,5	0,0	1,07	0,300	-	-	-
	colloid nodule	2,3	0,0	0,71	0,399	-	-	-
Presence of nodules		34,9	6,7	8,86	0,003	7,50	1,67	33,66
Classification of nodules TI-RADS	0	2,3	43,3	33,22	0,000	0,03	0,01	0,15
	1	55,8	56,7	0,01	0,935	0,97	0,42	2,23
	2	30,2	0,0	11,69	0,001	-	-	-
	3	10,5	0,0	3,40	0,065	-	-	-
	4	1,2	0,0	0,35	0,553	-	-	-
Vascularization	hypervascular	18,6	3,3	4,15	0,042	6,63	0,84	52,33
	hypovascular	5,8	16,7	3,33	0,068	0,31	0,08	1,15
	moderately vascular	75,6	76,7	0,01	0,905	0,94	0,35	2,51
Blood flow of nodules	perinodular	14,0	10,0	0,31	0,578	1,46	0,38	5,57
	intranodular	12,8	10,0	0,16	0,686	1,32	0,34	5,09
	Mixed	11,6	6,7	0,59	0,442	1,84	0,38	8,93

Note: χ2, P – reliability of differences in indicators of the compared groups according to the Pearson criterion

In a comparative analysis of the thyroid status of patients in the main and comparative groups, it was noted (Table 17) that despite the fact that most indicators (width, thickness, length of the right and left lobes, there were no significant differences (P>0.2; P>0 ,1), while a number of parameters (volume of the right and left lobe, thickness of the isthmus) were significantly greater in patients of the main group compared to the comparison group (P<0.05; P<0.01).

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Table 2. Comparative characteristics of thyroid ultrasound indicators in the examined main and control groups upon admission

№	Indicators	Main group (n=86))		Control group (n=30		P
		M	m	M	M	
1	Width of the right lobe	20,64	0,47	19,80	0,50	>0,2
2	Left lobe width	20,57	0,45	18,71	0,32	<0,01
3	Thickness of the right lobe	23,88	0,52	23,07	0,44	>0,2
4	Thickness of the left lobe	26,24	2,53	22,65	0,43	>0,1
5	Length of the right lobe	48,51	0,79	48,28	0,63	>0,5
6	Left lobe length	48,93	0,74	48,28	0,58	>0,2
7	Volume of the right lobe	13,35	0,67	11,39	0,63	<0,05
8	Volume of the left lobe	12,96	0,57	10,56	0,45	<0,01
9	Isthmus thickness	7,44	0,42	7,19	0,35	>0,5
10	Volume of the right lobe in total	18,27	0,37	17,43	0,27	>0,05
11	Volume of the left lobe in total	25,89	1,06	23,59	0,60	>0,05
12	Thyroid volume/body weight ratio	0,39	0,02	0,35	0,02	>0,1

Note: P – significance of the differences between the compared groups, according to the Student's test

To assess the effectiveness of the proposed therapy, a comparative analysis of the indicators of ultrasound examination of the thyroid gland in patients of the main group before and after treatment was carried out. The analysis showed (Table 20) that the treatment did not lead to significant results (P>0.5; P>0.2).

Table 3. Comparative characteristics of thyroid ultrasound parameters in those examined in the main group before and after treatment

№	Indicators	Main group (n=86) Before treatment		Main group (n=86) after treatment		P
		M	m	M	m	
1	Right lobe width	20,64	0,47	20,86	0,50	>0,5
2	Left lobe width	20,57	0,45	20,66	0,41	>0,5
3	Right lobe thickness	23,88	0,52	24,09	0,53	>0,5
4	Left lobe thickness	26,24	2,53	23,64	0,41	>0,2

5	Right lobe length	48,51	0,79	48,43	0,87	>0,5
6	Left lobe length	48,93	0,74	49,37	0,79	>0,5
7	Right lobe volume	13,35	0,67	13,43	0,65	>0,5
8	Left lobe volume	12,96	0,57	12,98	0,55	>0,5
9	Isthmus thickness	7,44	0,42	7,03	0,43	>0,2
10	The total volume of the left lobe	18,27	0,37	18,34	0,34	>0,5
11	Total volume of the right lobe	25,89	1,06	25,86	0,37	>0,5
12	Thyroid volume/body weight ratio	0,39	0,02	0,38	0,01	>0,5

Note: P – significance of differences before and after treatment, according to Student's test

Conclusions:

1. Thus, the use of expert systems to diagnose thyroid disorders is undoubtedly of interest to primary care physicians. In order to study and evaluate the function of the thyroid gland by physiologists and doctors, it is important to determine the secretion of thyroid hormones in the first place. The aim of our study is to study the prevalence of thyroid dysfunction, and to identify pathological conditions in the thyroid gland after coronavirus infection using ultrasound technology.

2. Based on the results of scientific research, it can be concluded that the infection of COVID-19 reduces the function of the thyroid gland, it is manifested by a decrease in the amount of free T4 and an increase in the amount of TTG. Elevated levels of anti-TPO, a marker of thyroid inflammation, are associated with decreased immune function and autoimmune inflammation in the thyroid after COVID-19 infection. Therefore, autoimmune thyroiditis is more common among thyroid diseases than other diseases.

3. Patients infected with coronavirus are more likely to develop thyroid diseases or dysfunction;

4. The presence of thyroid dysfunction does not increase the risk of acquiring SARS-CoV-2 infection;...

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