MINISTRY OF EDUCATION AND RESEARCH

INSTITUTE OF PHYSIOLOGY AND SANOCREATOLOGY

With manuscript title

C.Z.U: [612.44+611.411]:616.98:578.834.1-06:616.1/.8 (043.3)

CEBOTARI ANGHELA

THE PHYSIOLOGICAL AND ECO-MORPHOLOGICAL FEATURES OF THE THYROID GLAND IN THE POST-COVID-19 PERIOD

165.01 – HUMAN AND ANIMAL PHYSIOLOGY

Abstract of PhD Thesis in Biological Sciences

CHIŞINĂU, 2023

The thesis was developed within the Scientific-Methodological Center in Health and Biomedicine of the Institute of Physiology and Sanocratology of the State University of Moldova.

Scientific leader:
MEREUȚĂ Ion, qualified doctor in medical sciences, university professor.
Official references:
CRIVOI Aurelia, PhD in biological sciences, university professor, State University of Moldova.
COBEȚ Valeriu, PhD in medical sciences, university professor, "Nicolae Testemițanu" State University of Medicine and Pharmacy.

Composition of the Specialized Scientific Council:
BĂHNĂREL Ion, qualified doctor in medical sciences, university professor, "Nicolae Testemiţanu" State University of Medicine and Pharmacy (president);
POLEACOVA Lilia, doctor in biological sciences, Institute of Physiology and Sanocreatology (scientific secretary);
FURDUI Teodor, PhD in biological sciences, university professor, academician, Institute of Physiology and Sanocratology of the State University of Moldova;
STRUTINSCHI Tudor, PhD in biological sciences, associate researcher, Institute of Physiology and Sanocreatology of the State University of Moldova;
HALANGOT Nicolai, PhD in medical sciences, university professor, Institute of Endocrinology and Metabolism "V.P. Komosarenko", Kyiv, Ukraine;
MALÎGA Oxana, doctor of medical sciences, university lecturer, "Nicolae Testemiţanu" State University of Medicine and Pharmacy.

The defense will take place at December 22, time 14.00, in the Meeting of the specialized Scientific Council D 165.01-23-123 within the Institute of Physiology and Sanocratology of the State University of Moldova, 1 Academiei str., 3rd floor, conference room no. 352, Chisinau, Republic of Moldova.

The doctoral thesis and the abstract can be consulted at the "Andrei Lupan" Central Scientific Library (Chisinau, str. Academiei, 5A) and on the website of ANACEC.

The abstract was sent to "....." 2023.

Scientific Secretary of the Specialized
Scientific Council, doctor in biological sciences _____ **POLEACOVA Lilia**

Scientific leader, qualified doctor
in medical sciences, university professor _____ **MEREUȚĂ Ion**

Author _____**CEBOTARI Anghela**

CONTENT

CONCEPTUAL MARKINGS OF THE RESEARCH

Actuality and importance of the topic addressed. The disease COVID-19 is the pandemic of the new millennium. It can cause systemic inflammation, potentially leading to multiple organ dysfunction. Scientific data on the correlation between COVID-19 and the thyroid gland (GT) has emerged and grown rapidly since March 2020. GT is known to respond to infections. Upon infection SARS-CoV-2 reacts with immune inflammatory processes using ACE2 combined with transmembrane serine protease 2 (TMPRSS2) as a key molecular complex to infect host cells. ACE2 and TMPRSS2 expression levels are increased in GT and more than in lung [10]. During the COVID-19 pandemic, several papers reported that endocrine diseases and metabolic changes can be considered risk factors for acquiring the novel coronavirus. On the contrary, studies investigating whether SARS-CoV-2 can directly affect the endocrine glands, causing disorders that worsen the prognosis, are lacking. In post-mortem patient studies, both follicular and parafollicular cells of the GT were extensively affected in patients who died of SARS. In addition, ACE2 mRNA is present in thyroid follicular cells, highlighting the potential for thyroid cell entry by SARS-CoV-2, but to date no evidence of intracellular SARS-CoV-2 has been documented [12]. At the beginning of the pandemic, several cases of subacute thyroiditis were reported. Thyrotoxicosis was related to IL-6 levels, suggesting that patients with a higher inflammatory response were more likely to develop thyrotoxicosis [21]. In addition to subacute thyroiditis, there have been case reports of Graves' thyrotoxicosis in patients with COVID-19 who had no prior documentation of autoimmune thyroid disease. Viral infections can trigger the presentation of autoimmune thyroid disease; however, it has been postulated that the cytokine milieu induced by SARS-CoV-2 makes it a particular trigger for autoimmune thyroid disease. The nonthyroidal illness syndrome occurs during physiological stress and is characterized by an initial reduction in total T3 and fT3, with an increase in reverse T3, but without a concomitant increase in TSH [21].

Data on the involvement of GT in coronavirus infection are less. A study conducted during the SARS outbreak in 2003 reported that serum T3 and T4 levels were lower in SARS patients compared to patients in both the acute and convalescent phases. Follicular cell destruction would manifest as T3 and T4 hormone indices are low; parafollicular cell damage would theoretically lead to low serum calcitonin levels. Calcitonin deficiency leads to disinhibition of osteoclasts leading to osteoporosis and osteonecrosis.

To date, there are no data on direct damage to GT by the SARS-CoV-2 virus, however, the results of available studies and clinical observations indicate the potential effect of coronavirus infections, especially SARS-CoV and SARS-CoV- 2 on the hypothalamic-pituitary-thyroid axis

with the development of various pathologies or changes in the content of thyroid hormones (HT). The course of the disease of COVID-19 is associated with euthyroid disease syndrome or low T3 syndrome. In addition, changes in HT concentration can also be caused by the intake of glucocorticosteroids and anticoagulants. The manifestation of autoimmune thyroid diseases against the background of COVID-19 is also possible. Since GT has an important role on the body, participating in all its processes, some indices, including metabolism, in the formation of immunity, it was and is necessary to study how the SARS CoV-2 virus acts on GT. The need for the conducted study also required the study of the action of this virus on metabolism and eco-morphological and functional changes.

The aim of the paper is to evaluate the functional and eco-morphological peculiarities of the thyroid gland in patients infected with SARS CoV-2 in the post-COVID-19 period, as well as the way to promote physiological rehabilitation.

Research objectives:

1) Evaluation of the hormonal status of the thyroid gland in the pre- and post-COVID-19 period.
2) Echo-morphological highlighting of the thyroid gland in the pre- and post-COVID-19 period.
3) Estimation of some metabolic indices that reflect the danger of metabolic dysregulation, oxidative stress and the fibrosis marker (thymol test index) in patients with post-COVID thyroid gland disease.
4) Study of the dynamics of hematological changes in the post-COVID-19 period in patients with post-COVID thyroid gland disease.
5) Estimation of the psychophysiological status of patients with post-COVID-19 conditions of the thyroid gland.
6) The development of a phytotherapeutic food supplement, which would favor the physiological rehabilitation of the thyroid gland in the post-COVID-19 period.

Research hypothesis: It was based on the reaction of the thyroid gland to the damage caused by the disease COVID-19. The results of the investigations carried out can help the development of a faster diagnosis and a correct treatment in time for the disease of COVID-19, to stop the inflammatory and fibrosis process of the thyroid gland and the dysregulation of its function following this condition in order to avoid disability. COVID-19 is a systemic disease that influences the endocrine and metabolic-functional system that determines the state of human health.

Synthesis of research methodology and justification of chosen research methods. The scientific study and research methodology, which sums up a large number of contemporary methods used in this work, allowed the achievement of the proposed objectives and determined

the acquisition of new data that were the basis of the argumentation of the solved scientific problem. The scientific research methodology was based on the concepts regarding: 1) the basic principles of the periodization of the individual structural-functional development of the organism [6]; 2) the basic principles of physiology [1, 7]; 3) the basic principles of ultrasound and echo-morphology [5].

Summary of thesis sections:

The work includes: annotation presented in the languages: Romanian, Russian and English, list of tables, list of figures, list of abbreviations, introduction, four chapters, general conclusions and practical recommendations, bibliographic sources including 273 titles, acts of implementation of scientific results, declaration regarding the assumption of responsibility and the CV. The doctoral thesis is presented on 217 pages, the content of the thesis being completed with 29 tables and 52 figures.

THESIS CONTENT

1. THE PHYSIOLOGICAL AND ECO-MORPHOLOGICAL CHARACTERISTICS OF THE THYROID GLAND (LITERATURE MAGAZINE)

The chapter includes a deep analysis of the latest data from the specialized literature at the national and international bibliographic level. Scientific data on the normal anatomical and physiological aspects of the thyroid gland are presented. The synthesis and effects of thyroid hormones on carbohydrate, protein and lipid metabolism are described; classification of thyroid diseases, as well as general ultrasound and echo-morphology of the thyroid gland. The eco-morphological changes of the thyroid gland in the post-COVID-19 period are presented. The chapter ends with conclusions.

2. MATERIAL AND RESEARCH METHODS

The investigations, the results of which are presented in this paper, were carried out during the years 1992-2021. The current research represents a cross-sectional descriptive study, which was carried out within the AMT Centru, AMT Botanica Clinics and within the Institute of Physiology and Sanocratology (IFS). The research was carried out in accordance with the Study Design adopted by the Scientific Research Ethics Committee of the Institute of Physiology and Sanocreatology (Opinion of the Scientific Research Ethics Committee of IFS (Minutes no. 15 of 25.02.2021)). The data collected from the study surveys and from the Statistics Office of the CSP of the ANSP of the MSRMPS were also used. The descriptive study was carried out, according to the study sample, but also the selective study in accordance with the Epi-INFO Program 7.2.2.6 for cross-sectional study in accordance with the following parameters and the identification of a

number of 5705 subjects with thyroid gland pathologies during the years 1990- 2002. In connection with the study of post-COVID-19 consequences, 496 subjects were examined, who in 2018-2019 were without thyroid gland disorders, and during the years 2020-2021 the same subjects with post-COVID-19 consequences. Out of 496 subjects, 3 subjects went abroad and 11 subjects refused (did not show up). From which the proportional stratification after COVID-19 was performed at one month, at 6 months and at 12 months for 482 subjects. Inclusion criteria in the study: 1. Respondents, subjects who underwent an ultrasound examination during the years 2020-2021, who endured the disease of COVID-19, were examined at one month, at 6 months and at 12 months in the post-COVID period -19; 2. Respondents aged >20 years and <60 years; 3. Respondents who have given informed consent; 4. Respondents who were examined ultrasonographically and confirmed with COVID-19; 5. Respondents' consent to the processing of medical and personal data. Exclusion criteria: 1. Respondents who requested exclusion from the study at any stage of the study; 2. Respondents aged <20 years and >60 years; 3. Respondents with a damaged somato-functional background due to concurrent illnesses in the sub- and decompensation phase.

The results presented in the given study were obtained from the examination of 15,000 subjects (in the years 1992-2021), of which 5705 with thyroid gland disorders and 482 (100%) subjects (2018-2021, who represent the subjects of the ultrasound examination from the Medical Institutions Registers. Average age groups 20-60 years. Men – 226 (46.89±2.8) and women – 256 (53.11±3.7). The characteristics of the subjects showed the predominance of age between 40-50 years and 50- 60 years old, of which men 158 (70%) and women 167 (65%). Classical and modern study methods were used, including: hematological methods for analyzing blood indices; biochemical methods for studying the state of protein, carbohydrate and lipidic; hormonal investigation methods for the determination of thyroid hormones; immunological investigation methods for determining the immune status of the research subjects; ultrasound methods for assessing the eco-morphological state of the thyroid gland; the questionnaire – research method of the psychophysiological peculiarities of the research subjects; statistical methods of results analysis.

3. STRUCTURE AND PHYSIOLOGY OF THE THYROID GLAND IN THE PRE-COVID-19 PERIOD

3.1. Structural, physiological changes, parameters and abnormalities of the thyroid gland.

Normal thyroid tissue has homogenous echogenicity and echostructure. In longitudinal section, the thyroid lobe is ovoid, sometimes triangular. The anterior surface of the GT in the

region of the isthmus is often confused with the echoes coming from the skin surface, but the acoustic shadow of the trachea can help us in demarcation. Carrying out the investigation on 1546 patients [5] and, based on the results of other additional methods to be investigated, it was concluded that GT is not the same for everyone. It can differ in shape and size. The parameters of the right lobe can be 1-2 mm larger than those of the left lobe. Women's sizes are smaller than men's. In some subjects the thickness of the lobes may vary, less or more, by 1; 2; 3; 4 mm. In children - no deviations. Echoscopic GT is of three shapes: conical, triangular and flat depending on the constitution. This is of great importance, because errors can be avoided and even the smallest condition (hyper- or hypoplasia) can be detected in time. It was found that until the age of 16-20 years, the dimensions of the gland grow quickly, from 20-60 years - the dimensions are stable, after 60 - they decrease. The volume determined by palpation was overestimated in 27% and underestimated in 8% of cases. The structure can be: homogeneous micronodular, inhomogeneous, with formations and without - depending on the patho-morphological processes, the tissue can have medium, increased, low or mixed echogenicity.

3.2. Pathophysiology and semiology of the thyroid gland.

The physiopathology of thyrotoxicosis is explained by the excess of HT in the blood circulation and etiopathogenetic peculiarities, and the myxedema in the deficiency of HT in the blood circulation, the tissue resistance to the action of these hormones, the disturbance of the conversion of T4 into T3.

General sonographic semiology of GT. For an organ with a solid structure, the contour, dimensions, volume, shape, structure and relationship with neighboring organs are systematically described. The outline can be well or poorly defined (confused), linear or bumpy. The shape of GT, according to the results of echoscopic research, depending on the constitution of the body, it was found that it can be of three types: conical, flat and triangular [5]. Respectively, they were presented in the following proportions: 1) conical - 8-10%; 2) payment – 10-12%; 3) triangular – 75-80%. The dimensions were measured at the level of the conventional anatomical areas, initially established by the separate evaluation of each lobe. The measurements are performed on the three axes: sagittal, transverse and vertical. Any change in dimensions that have certain limits, denotes a pathological process.

Different pathologies were detected depending on age and sex. It is confirmed that the percentage of pathology in women is higher than that detected in men. At the same time, depending on age, subjects between 30-50 years of age are most affected, with a decrease in pathologies at 60 years of age. Changes in the structure express changes in the anatomical state of the organ: circumscribed or diffuse, liquid, solid or mixed. The liquid ecostructure on the monitor screen is

presented through a pure transonic image with an isoelectric line at the level of the rear wall. These echoes give evidence of a process of necrosis, especially if they are of different intensity. The solid-type ecostructure in GT has a variable appearance, depending on the morphopathological nature of the lesions. The solid lip ecostructure can be micro- or macronodular, homogeneous or non-homogeneous, hypo-, hyper- or heterogeneous, with a well- or poorly defined, regular or irregular outline. The mixed ecostructure is characterized by associations of transonic and reflectogenic elements. Anatomically-patho-morphologically, they are the expression of fibrous tissue alterations with areas of necrosis. Beaches of solid tissue are associated with liquid. Depending on the stage of the process, hyper- or hypoechoic areas may predominate [5].

Ultrasound semiology of blood vessels is specific and depends both on the anatomical structure and existing pathologies (thyroiditis (acute, subacute (autoimmune, fibrous, chronic, specific – tuberculous, echinococcosis and others)). Local thyroid changes are determined by physiopathological mechanisms of inflammation in acute and subacute forms. In chronic thyroiditis, the local phenomena have an autoimmune mechanism with a characteristic lymphoplasmacytic infiltrate and two local forms of manifestation: with gout, (hypertrophic) or atrophic. We have determined the inflammatory processes that can be: A) acute - hypertrophy thyroid accompanied by an extremely intense process; B) subacute - with local manifestations and thyroid hypertrophy of lower intensity: a) in acute thyroiditis, the acute inflammatory process leads to the massive destruction of thyroid follicles, with the quantitative release of HT, with the appearance of thyrotoxicosis. In a short time there is a decrease in deposits and the appearance of hypothyroidism; b) in subacute thyroiditis, the partial destruction of the thyroid follicles occurs with the release of HT from the gland's deposit and, consequently, after exhaustion – hypothyroidism; C) chronic, lymphocytic thyroiditis occurs as a result of hormone biosynthesis disorders, iodine organization defect, abnormal release of iodoproteins. Over time, thyroid lesions progress, the concentration of thyroid hormones decreases, subsequently with a decrease in GT reserves (hypothyroidism).

An increased percentage of GT diseases was attested, of which grade I and II hyperplasia occupies 12.6%; Diffuse grade III and IV goiter – 3.6%, including formations – 0.5%; Toxic diffuse goiter – 2.1%; Hashimoto's goiter – 5.5%; Riedel goiter – 0.4%; formations in the focus – 12.3%, of which nodules – 4.8%, adenoma – 2.7%, cyst – 1.5% and tumor – 1.5%; postoperative condition – 1.3% and recurrences – 0.5%. At the same time, it is observed that the number of female subjects in all types of detected conditions is higher than in males. This deviation is explained by more frequent addressing and investigations in women, the change in the hormonal background following pregnancy, as well as the genetic transmission from mother to daughter.

3.3. Ultrasound classification of nodules and other thyroid conditions in the pre-COVID-19 period.

Following the investigations, 4 types of changes (hyperplastic) were observed in the glandular tissue: 1. Diffuse enlargement of GT without nodular formation(s). This condition is characterized by a diffuse increase in volume or due to a lobe of the thyroid gland with a changed ecostructure (hypo-, hyper-, hetero-) without nodules; 2. Diffuse increase in volume of GT with nodular formation(s). Diffuse or partial enlargement of the thyroid gland with a change in ecostructure (hypo-, hyper-, hetero-) and the presence of one or more nodules in the tissue is characteristic; 3. Nodular formation of GT. This lesion is characterized by the presence of a nodule, in any division of the thyroid gland against an unchanged tissue background; 4. Nodular formations of GT. It is characteristic of the presence of several nodules in any division of the thyroid gland or throughout it, against the unchanged background of glandular tissue of different shapes and sizes [5].

After the performed investigations (punctures), the following pathomorphological changes of the nodules with sizes up to 10 mm and more were observed. Nodules with a diameter of up to 10 mm have a homogeneous internal structure, this means that they have the same morphology; given the fact that the blood circuit is satisfactory, trophic, degenerative changes and cavities of destruction - are missing; microcalcinates or different structure were not found in these nodules; in nodules up to 10 mm no microfoci of malignant tumors were found, if so – then the whole nodule (papillary cancer). Nodules with a diameter greater than 10 mm can have both homogeneous and non-homogeneous ecostructure, which will also make the morphological structure different; some pathomorphological changes may be present in them, for example: thyroiditis + goiter + papillary cancer microfocus; all the blood disorders in the node lead to trophic changes, which makes it obvious that the morphological structure is also changed [5]. In this case, it is desirable to score from several places (from the center and the periphery).

Diseases of the thyroid gland. During the examination of the research subjects, a series of conditions of GT were detected such as:

Diffuse (toxic) goiter (Bazedow's disease, Graves' disease, Parry's disease) is conditioned by the exaggerated secretion of HT by diffusely enlarged GT, histologically with diffuse hyperplasia.

Diffuse nodular (multinodular) goiter that usually develops at the age of 50-60 years, but our research determined cases at the age of 22, 25, 30 years with frequent thyroid nodules in 47%, predominantly in women.

The cyst, a transonic formation with posterior attenuation of round or oval shape, with thin walls and colloidal content, sometimes with hemorrhagic content, or sediment (which changes its place and shape when the body position changes), with a very sensitive echosecretion for detecting lesions, identification of cystic nodules of 2 mm and solid nodules of 3 mm.

Suppurative thyroiditis, after angina, furunculosis, sepsis, pneumonia, tonsillitis, with an ultrasound in the acute moment is represented by diffuse hyperplasia of the thyroid gland.

Subacute thyroiditis (De Quertain's Thyroiditis), an inflammatory process of the thyroid gland, of viral etiology, occurs more frequently in women, having a moderate hypertrophy of the gland and an inconsiderable inflammatory reaction.

Fibrous thyroiditis (Riedel thyroiditis), which is characterized by GT hypertrophy, the normal structure of which is replaced by fibrous tissue with damage to the stroma and its capsule. Echoscopically, initially GT has diffusely enlarged dimensions or of a lobe. The structure, initially relatively homogeneous, becomes inhomogeneous with a network of reflectogenic threads like a "spider", partially or throughout. The irregular (confused) contour gives the impression of concretion with the neighboring tissues. It is hard on examination and is not mobile during the act of swallowing. Parallel to the changes in the gland, changes in fibrosis are detected in other organs as well.

Autoimmune thyroiditis (lymphogranulomatous) (Hashimoto's), common at the age of 40-50 years, even younger, including children. From the number of patients suffering from this disease, according to the investigations carried out, children make up 38%. The disease occurs more often in women. Autoimmune thyroiditis affects approximately 10-12% of the population, the female predominance being clear (the ratio of women/men is 9/1) autoimmune thyroiditis evolves with hypothyroidism in 3%-20% of cases. Two forms are characteristic of the disease in question: hypertrophic and hypotrophic. In the hypertrophic form of autoimmune thyroiditis, the thyroid gland is enlarged, and in the hypotrophic form – the dimensions are normal or even reduced. The decrease in gland function is characteristic for both forms of autoimmune thyroiditis, although the hypertrophic form of autoimmune thyroiditis, in the first years of the disease, may result in thyrotoxicosis phenomena. Echoscopically: the disease in 92% is presented by variable sizes of the thyroid, more often - small volume. The outline is often irregular. The pronounced inhomogeneous, diffusely modified structure is hardly perceptible. Echogenicity is globally reduced with the presence of some pseudonodules (hypoechoic beaches) of an irregular chaotic shape, sometimes with strands of fibrosis. Calcifications can often occur.

Hypothyroidism is manifested by the decrease of GT function. We distinguish between primary, secondary and tertiary hypothyroidism. Secondary hypothyroidism usually presents with

various anatomical and structural changes of the anterior pituitary lobe, and in tertiary hypothyroidism it remains intact. Primary hypothyroidism is conditioned by the following causes: a) developmental anomalies of the thyroid gland (dysgenesis, ectopy); b) endemic goitre and cretinism; c) inflammatory diseases of the gland (Riedel, Quervain thyroiditis, Hashimito autoimmune thyroiditis); d) thyroidectomy; e) radioactive iodine therapy; f) dysregulation of the biosynthesis of thyroid hormones; g) thyrostatic drug therapy. Primary hypothyroidism is reported in 95% of subjects and secondary and tertiary hypothyroidism in only 5%. The basis of the development of hypothyroidism is the long-term and considerable deficit of the specific action of thyroid hormones in the body with the reduction of oxidative and thermogenesis processes, the accumulation of metabolism products, which leads to functional disorders of the CNS, endocrine, cardiovascular, digestive systems, etc., as well as dystrophy and mucoprotein edema, specific to different tissues and organs. Echoscopically, this disease, depending on the cause that led to it, has variable images. If hypothyroidism was caused by a condition of the thyroid gland such as Riedel's thyroiditis, Hashimoto's thyroiditis, the image of the gland will usually have reduced dimensions. The outline can be irregular, sometimes confusing, the tissue structure is almost not visualized (depending on the stage of the disease), pronounced inhomogeneous, more often predominantly hypoechoic.

Adenoma that occurs 3-5 times more frequently in women of different ages, sometimes also in children. Thyrotoxic adenomas are usually not too large, 2-3 cm in diameter, while solitary euthyroid nodules are 4-5 cm in diameter. Echoscopically, this disease is presented by one or more formations that appear on the unchanged background of the ovoid-shaped tissue, sometimes compressing the neighboring tissues. Adenoma can be: follicular, papillary, atypical and medullary. The contour is usually well highlighted, sometimes weak, regular, uninterrupted. The internal structure can be homogeneous, hyperechoic or mosaic with micro- or macro-nodules, with cystic degeneration. Poorly defined lesions can be distinguished from glandular tissue by the presence of the so-called "halo", which is signaled by a uniform hypoechoic zone of 1-2 mm width, characteristic of benign formations. Adenomas with a mixed structure are more common (where tissue and cystic degenerations, hemorrhages, fibrosis, and sometimes calcifications are also present). Sometimes several adenomas can be found in a gland at the same time, with different histological structure. The smallest adenomas are located in the thickness of the tissue, but as they grow, they move to the periphery of the lobes. Special attention should be drawn to the "halo", because it is also found in malignant formations, but, unlike the adenoma, the "halo" is uneven and interrupted.

Diffuse pseudoadenomatous goiters are adenomas and are characterized by focal hyperplasia or diffuse colloidal degeneration.

GT tumors are divided according to histological signs into benign and malignant. The most common tumors are found in women. Malignant thyroid tumors are variable: 90% of them are adenosarcomas, malignant lymphoma, fibrosarcoma, metastases of other cancers, etc. The most common thyroid cancers are differentiated epithelial ones, which have a structure similar to thyroid follicles. According to the anatomopathological aspect, the following types of tumors were observed: papillary carcinoma, follicular carcinoma, anaplastic carcinoma, medullary carcinoma, malignant lymphoma. Thyroid cancer is a model of endocrine cancer. Currently, cases of thyroid cancer are also frequently encountered in young patients, which manifest respectively through differentiated thyroid carcinoma. At an older age, undifferentiated thyroid carcinoma begins - one of the most aggressive and malignant human adenocarcinomas, which, fortunately, is rarely encountered. Follicular carcinoma has a higher incidence in iodine-deficient areas, while papillary cancer is associated with a normal or increased iodine level.

Follicular cancer occurs in adults. It is characterized by slow growth. Approximately 40% of cases metastasize in bones, brain, lungs, invade neck muscles, trachea. In the thyroid gland it appears as a mobile nodule.

Medullary cancer is characterized by the presence of fibrosis and exaggerated ameloid agglomeration, sometimes with calcification phenomena, other times with a familiar character. It can be associated with parathyroid and adrenal hyperplasia. The disease can also be associated with pheochromocytoma, neurofibromatosis, parathyroid adenoma (multiple endocrine adenomatosis type II). They can be accompanied by the clinical picture of Itenko-Cushing syndrome. Medullary cancer is a solitary tumor, which develops slowly in the form of a GT nodule with metastases in internal organs.

Anaplastic cancer grows rapidly, infiltrating adjacent structures, leading to death within a year. It attacks a lobe or the entire gland.

Papillary cancer also occurs in children, but more frequently in adults. It presents itself as a nodular goiter that develops slowly, metastasizing very quickly in other organs. It concretizes with the capsule and adjacent tissues. Metastases of malignant tumors in the thyroid are less common. Such tumors include melanoma, breast, gastric, pancreatic, intestinal cancer, as well as lymphomas. The primary focus is difficult to locate. The clinical picture of thyroid cancer is very often represented by a single painless nodule, more often identified by chance in other organs. The GT tumor can reach large sizes, fixing the trachea and causing dysphagia, dystonia or hoarseness of the voice. Many times the picture of thyrotoxicosis can be present. Thyroid cancer is necessary

to differentiate it from the solitary nodule and the multinodular goiter, adenomas, metastases. Often it can be associated with Hashimoto's goiter or diffuse toxic goiter. The number of thyroid cancer cases in the last ten years has increased significantly (from 7-8% to 10-15%). Echoscopically, this disease appears on the monitor screen in the form of a nodule, cyst or several foci. Echogenic masses with a capsule thickness greater than cysts - suggest the presence of a neoplasm. The presence of a mass with thickened walls, with numerous inclusions (internal echoes), especially if it is poorly defined, a carcinoma can be suspected. The smallest formation detected by ultrasound was 5 mm. Sometimes the formation can have voluminous dimensions. The location can be different and so can the progression. If at first the formation can be taken as a nodule, adenoma or cyst, then other signs of distinction between a benign mass and a malignant one appear. The results of the anatomopathological ultrasound investigation of the tumor formations were confirmed by biopsy.

3.4. Pathological changes of internal organs in subjects with thyroid gland conditions in the pre-COVID-19 period.

In the same subjects with thyroid conditions, diseases of the internal organs were also detected:

a) The liver. Echoscopic changes are in the form of hepatosis and diffuse changes in the focus. The liver is enlarged, the marginal angles of both lobes are rounded; liver parenchyma with increased reflectivity, posterior attenuation of echo signals, increased reflectivity along the route of cross-sections of bile duct vessels, signs of liver tissue fibrosis. Less often – hemangiomas, calcifications, cysts, tumor formations.

b) Cholecystitis following diseases of the thyroid gland, which, echoscopically, manifests as a normal or deformed shape, with folds and a septum in the region of the body and neck, which cause swelling and which further predispose to the formation of stones following the deterioration of the evacuation of the liver. The walls are reflective, sometimes thickened, more frequently, due to biliary stasis, in the cavity (lumen) sloped sediment and vesicular biliary lithiasis are detected in 23%, less often - polyps, tumor formations, there can be multiple stones that block the function of the cholecyst "cholecyst disconnected". Gallbladder microlithiasis is more common, gallbladder polyps are less common.

c) The pancreas. The conditions of this organ are represented echoscopically by diffuse echoes in the structure, sometimes pronounced reflectogenic, which are difficult to differentiate from other conditions of this organ, but clinically, most of the time, patients do not present accusations. Currently, being described and treated as pancreatitis. These diseases of the pancreas were found in 36% of the examined cases.

d) The kidneys mostly undergo changes in subjects with GT conditions. More often, the formation of oxalate, urate, phosphate stones of various sizes occurs. Salts and stones periodically form and periodically, if they are small in size, they are easily removed with urine. Rarely, we encounter coralliform stones that are difficult to treat and block the function of the kidneys. Following the evacuation of microlithiasis or renal lithiasis, post-inflammatory sequelae are formed. Kidney lesions are clinically presented by various disorders, changes in the secretory function of urine, pyelocalyceal hypotonia and stasis, blood pressure disorders (predominantly increased). Echoscopically, kidney diseases are manifested by a picture characteristic of chronic pyelonephritis. Renal sinus of inhomogeneous structure with signs of post-inflammatory sequelae, in some chronic cases with signs of sclerosing, pyolocaliceal dilatations of various degrees, accompanied by microlithiasis and renal lithiasis. Cysts and tumor formations are less common. Kidney diseases constitute 47% of cases.

4. ECO-MORPHOLOGICAL AND PHYSIOLOGICAL PARTICULARS OF THE THYROID GLAND IN THE POST-COVID-19 PERIOD

4.1. Physiological and eco-morphological state in subjects infected with the COVID 19 disease.

For the anatomical highlighting, the volume of the GT, the determination of the physiological function, the hormones T3, T4, TSH depending on age, sex, weight, 100 subjects were examined - 50 women and 50 men grouped in the age groups of 20-30, 30-40, 40-50 and 50-60 years. An increasing trend of GT sizes was observed in the age groups of 20-30, 30-40 and 40-50 years, and a decreasing trend in the age group – 50-60 years. This feature is specific to both GT and isthmus lobes. Several factors are known to be involved in the regulation of GT volume, and the most studied are the effects of iodine on GT [11].

The study of GT volume depending on sex and age determined that GT in men had an average volume of 21.5±1.12 mm3, and in women – 17.5±1.08 mm3. The level of HT in men was found to be lower than in women, both T3 and T4, while the amount of TSH, conversely, decreased. In men, the T3 hormone level was 2.1±0.98, and in women – 2.22±1.04 nmol/L; the T4 level in men was 101±11.8, and in women 128±14.9 nmol/L. The TSH level in men was 2.75±1.3 and in women – 2.35±1.2 nmol/L. Studies on GT volume and HT depending on age groups, but also selective sex, have significantly demonstrated that both volume and function are different in various age groups. GT volume has an increasing curve with age and, after 60 years, the volume decreases reaching up to 18.01±0.1 mm3. In men, the indices were increased by 1.2±0.3 mm3, compared to women.

The average indices of HT T3 and T4 studied showed increases. The level of the T3 hormone in men increased by 0.12±0.02 nmol/l compared to women, and the T4 hormone caused a decrease in the 20-30 year group compared to the 50-60 year group from 106.0± 22.8 to 153.4±21.12 nmol/l. There are several studies investigating an association between thyroid volume (VT) and body weight. Most recent reports attest that VT is significantly correlated with body weight and body mass index (BMI) [18]. On the other hand, in some studies, only low body mass was found to be associated with VT. However, regarding thyroid function, results are conflicting in the literature with higher, lower or similar levels of HT in obese compared to normal weight subjects [14]. GT increases in volume depending on the age group by 3.01 mm3. This conclusion is necessary for the anthropological correlation of GT depending on age, weight and pathology. A sex-dependent positive correlation between GT volume and body weight was observed, which explains that the higher body weight of men is involved in the sex difference in thyroid size.

4.2. The eco-morphological peculiarities of the thyroid gland in the post-COVID-19 period.

The ultrasound examination in the post-COVID-19 period was performed at one month, at 6 months and at 12 months, the subjects being grouped as follows: 12 (2.48%) – up to 20 years; 58 (12.03%) – 20-30 years old; 87 (18.04%) – 30-40 years old; 151 (31.32%) – 40-50 years and 174 (36.12%) – 50-60 years. Women constituted a total of 256 (53.11%), and men – 226 (46.89%). One month after the post-COVID-19 period, GT, in the vast majority of cases, remains with pronounced edema, with increased dimensions, characterized as diffuse hyperplasia of the II-III degree, clear outline, relatively homogeneous structure, but with echogenicity reduced, which is characteristic of thyroid tissue edema.

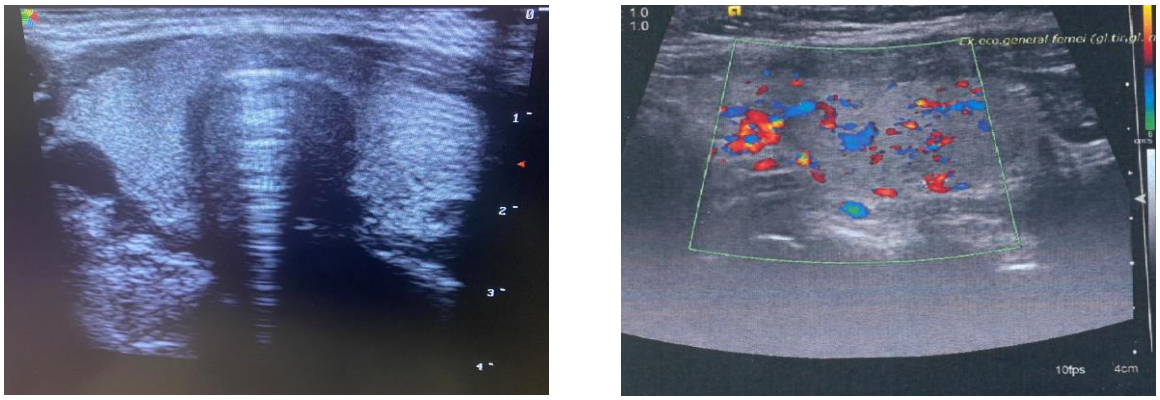


Fig. 4.1. The presence of edema, hyperplasia at one month of the post-COVID-19 period and the presence of increased vascularization *(original)*

In Figure 4.1. edema, low echogenicity and increased vascularity are observed in this post-COVID-19 period. Changes in the function and structure of thyroid tissue may occur during COVID-19 as a consequence of direct or indirect effects of SARS-CoV-2 infection on GT. On the

one hand, SARS-CoV-2 uses ACE2 as a receptor to infect host cells, and ACE2 is highly expressed by follicular thyroid cells. Thyroid disorders related to COVID-19 include destructive thyroiditis and the onset or recurrence of autoimmune disorders of GT, leading to a wide spectrum of thyroid dysfunctions, from thyrotoxicosis to hypothyroidism, which may worsen the clinical course of COVID-19 and affect prognosis [22] . In the period of 6 months post-COVID-19, GT sizes tend to decrease, reaching the physiological norm of the age group. The outline becomes bumpy, and the structure is inhomogeneous, the tissue structure is difficult to perceive, with predominantly hyperechoic tissue areas and signs of fibrosis (Figure 4.2.).

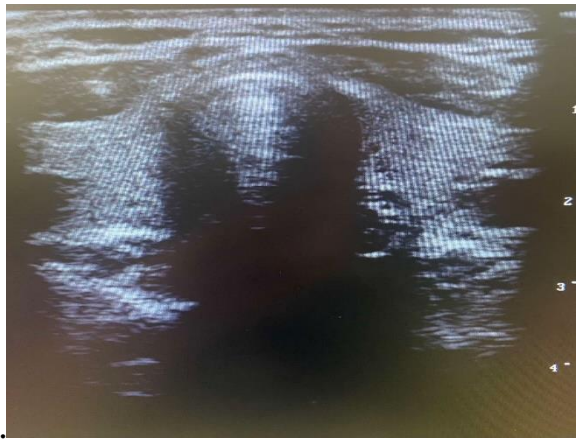
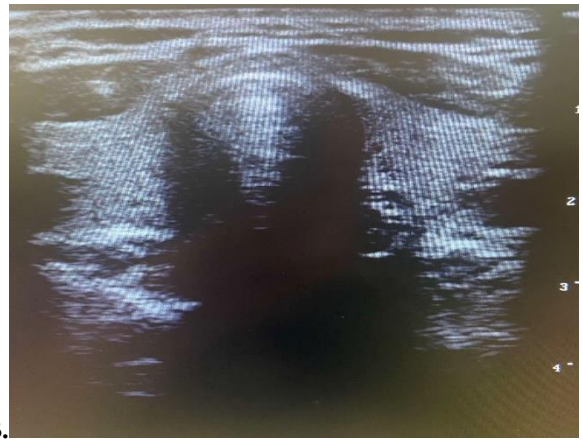
A.  **B.** 

Fig. 4.2. The presence of increased echogenicity (A) and the beginning of sclerosing (B) at 6 months of the post-COVID-19 period *(original)*

It has been proven that in the case of subacute thyroiditis associated with the COVID-19 infection, the thyroid ultrasound examination shows a diffuse increase in vascularity and a heterogeneity of the parenchyma. At 12 months post-COVID-19 on the background of fibrosis, GT shrinks, atrophy of the glandular tissue with connective tissue substitution and fibrosis process is observed (Figure 4.3.).

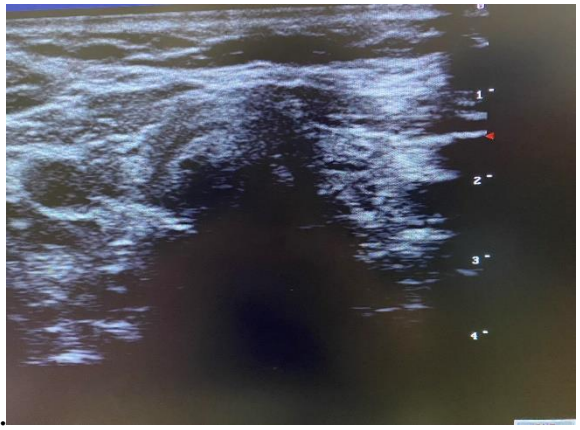
A.  **B.** 

Fig. 4.3. Presence of sclerofibrosis (A) and thyroid gland shrinkage (B) at 12 months post-COVID-19 (original)

It should be noted that GT atrophy occurs not only in terms of volume (Figure 4.3.), but also in terms of functionality, the clinic of hypothyroidism appears - weight gain, slowness in movements, in thinking, memory and concentration disorders, asthenia, depression, feeling of a lump in the throat and suffocation, constipation, etc. Metabolism is disrupted and type II diabetes occurs. The volume of GT in subjects researched in the post-COVID-19 period has a gender-dependent dynamic: it is higher in men than in women. GT volume also differs depending on age, being higher at 30-40 years and lower at 50-60 years. At one month being with a higher volume, than at the sixth and 12th month of the post-COVID-19 period. The increase in volume is explained by the manifestation following edema, being a consequence of post-COVID-19 complications, of the autoimmune reaction depending on the severity of the infection and the adaptation period.

Following investigations from the total number of subjects, a case of thyroid tissue change with hyperplasia was detected, after 12 months, signs of tumor formation appeared against the background of changed tissue. Some reasons for the appearance of the possible tumor formations detected as a result of the analysis of the investigations carried out, may appear as a result of the resulting hyperplasias, the decrease in immunity and the post-traumatic stress suffered as a result of the COVID-19 infection.

4.3. Hormonal peculiarities of the thyroid gland in the post-COVID-19 period.

Physiological indices in the subjects studied during the years 2019-2021 depending on age, of the level of thyroid hormones (Table 4.2., 4.3., 4.4.) had conclusive values.

At the age of 20-30 years, the concentration of the T3 hormone in women is 2.20±0.05 and in men – 2.14±0.10 nmol/L; of the T4 hormone in women is 106.50±22.80, and in men – 108.30±20.10 nmol/L; of TSH in women is 2.30±0.06 and in men – 2.40±0.30 nmol/L.

Table 4.2. Thyroid hormone T3 content in blood, post-COVID-19 period

Age (years)	Gender	The established norm (nmol/L) (n=482)	1 month (nmol/L) (n=482)	6 months (nmol/L) (n=482)	12 months (nmol/L) (n=482)
20-30	F	2,20±0,05	2,40±0,06*	2,30±0,17	1,10±0,17*
	M	2,14±0,01	2,38±0,11*	2,2±0,19	1,20±0,11*
30-40	F	2,30±0,19	2,39±0,17	2,37±0,04	1,20±0,14*
	M	2,35±0,19	2,40±0,08	2,31±0,06	1,12±0,17*
40-50	F	2,30±0,08	2,39±0,11	2,30±0,07	1,20±0,13*
	M	2,30±0,12	2,38±0,09	2,30±0,08	1,20±0,11*
50-60	F	1,84±0,08	1,98±0,01	1,34±0,09*	1,11±0,14*
	M	1,96±0,12	2,00±0,09	1,98±0,07	1,14±0,13*

Note: * - significant comparative differences ($p<0.05$)

At the age of 30-40, the T3 hormone level in women is 2.30±0.19, and in men 2.35±0.19 nmol/L; the concentration of the T4 hormone in women is 147.80±24.60, and in men – 148.40±22.80 nmol/L; of TSH in women is 2.40±0.10, and in men – 2.50±0.03 nmol/L.

Table 4.3. T4 hormone content of GT in blood, post-COVID-19 period

Age (years)	Gender	The established norm (nmol/L) (n=482)	1 month (nmol/L) (n=482)	6 months (nmol/L) (n=482)	12 months (nmol/L) (n=482)
20-30	F	106,50±22,80	108,40±21,60	77,30±11,90	50,30±1,30*
	M	108,30±20,10	109,00±22,40	78,40±29,30	50,50±1,10*
30-40	F	147,80±24,60	149,00±19,60	74,60±11,90*	52,10±1,10*
	M	148,40±22,80	150,00±17,30	79,00±18,70*	51,20±1,20*
40-50	F	151,30±18,40	152,00±18,90	72,60±22,10*	50,40±1,80*
	M	153,40±21,60	154,60±15,30	74,80±19,30*	52,10±1,20*
50-60	F	152,20±17,90	153,40±18,90	73,70±19,30*	52,10±1,30*
	M	153,40±19,40	154,60±12,10	74,90±11,90*	52,10±1,10*

Note: * - significant comparative differences ($p<0.05$)

At the age of 40-50 years, the HT T3 concentration in women is 2.30±0.80, and in men – 2.30±0.12 nmol/L; the HT T4 level in women is 151.30±18.40, and in men – 153.40±21.60 nmol/L; the concentration of TSH in women is 2.50±0.80, and in men – 2.30±0.30 nmol/L.

Table 4.4. Thyroid hormone TSH content in the blood, post-COVID-19 period

Age (years)	Gender	The established norm (nmol/L) (n=482)	1 month (nmol/L) (n=482)	6 months (nmol/L) (n=482)	12 months (nmol/L) (n=482)
20-30	F	2,30±0,06	3,30±0,07*	8,40±0,90*	11,50±0,70*
	M	2,40±0,30	3,40±0,06*	8,50±0,50*	11,60±0,70*
30-40	F	2,40±0,10	3,40±0,09*	3,50±0,07*	10,80±0,90*
	M	2,50±0,03	3,50±0,08*	8,60±0,90*	11,20±0,80*
40-50	F	2,50±0,80	3,50±0,60	8,60±1,20*	12,10±1,10*
	M	2,50±0,30	3,50±0,50	8,60±0,90*	11,30±1,20*
50-60	F	2,50±1,40	3,50±1,60	8,60±1,90*	11,20±1,30*
	M	2,40±1,50	3,40±1,90	8,50±0,80*	11,70±1,10*

Note: * - significant comparative differences ($p<0.05$)

At the age of 50-60 years, the T3 value in women is 1.84±0.80, and in men -1.96±1.20 nmol/L; T4 concentration in women is 152.20±17.90, and in men – 153.40±19.40 nmol/L; the TSH level in women is 2.50±1.40, and in men – 2.40±1.50 nmol/L.

The data of a study shows that in the post-COVID-19 period, a decrease in TSH indices was observed, and later its values returned to the initial value, suggesting that the changes are reversible with the recovery from COVID-19. The decrease in the level of TSH in patients with COVID-19 can be explained by the direct damage to the follicles or by pituitary dysfunction [19]. Patients with COVID-19 who have been diagnosed with pathological euthyroid syndrome, characterized by a low serum level of T3 and T4, without an increased secretion of TSH, may be caused by the direct action of SARS-CoV-2 on thyroid cells. SARS-CoV-2 infection can lead to downregulation

of 5'-deiodinases activity, with low T3 levels. COVID-19 causes a negative nitrogen balance and protein consumption that can lead to decreased serum levels of HT transport proteins, inhibiting T4 transport to T3-producing tissues. In a limited number of cases of subjects infected with COVID-19, decreased serum levels of T3, T4 and TSH have been detected. Evaluations of GT function showed thyrotoxicosis, with suppressed serum TSH, elevated levels of T4L, T3L and thyroglobulin, as well as the absence of thyroid autoantibodies [23].

4.4. Dynamics of biochemical indices in subjects with echo-morphological changes of the thyroid gland in the post-COVID-19 period.

The activity of alanine aminotransferase (ALT), which catalyzes the reversible reaction of the transfer of amino groups from alanine to oxoglutarate with the production of glutamate and pyruvate, as well as the activity of aspartate aminotransferase (AST), which catalyzes the reversible transfer of the amino group from L-aspartic acid to 2- oxoglutaric had a tendency to decrease both at 6 months and at 12 months of the post-COVID-19 period, compared to the first month of the research period, which is consistent with data from the literature where in the case of the disease of COVID-19 s -attested increases in AST and ALT [24].

The indices of γ-glutamyltranspeptidase, urea, total bilirubin, indirect bilirubin, albumin, creatinine, cholesterol and triglycerides did not undergo changes, remaining practically at the level of the indices of the first month of the post-COVID-19 period. Glucose level decreased at 6 and 12 months post-COVID-19 compared to first month indices. In the specialized literature, in non-diabetic people with the disease of COVID-19, high levels of glucose have been attested, which may be partially caused by the reduced consumption of glucose by the cells [17]. Coagulation time also remained unchanged. Total protein content also decreased significantly at 6 months and 12 months post-COVID-19 compared to the first month. The prothrombin index decreased truthfully at 12 months of the post-COVID-19 period, compared to the first month (72.00±0.23 ($p<0.05$)) [4]. Analyzing the changes in biochemical indices, a direct correlation between thyroid conditions and biochemical changes is attested, which would provide the opportunity to make a correct diagnosis and improve the treatment of post-COVID-19 complications.

4.5. Dynamics of hematological indices in subjects with echo-morphological changes of the thyroid gland in the post-COVID-19 period.

The most relevant decreases were found in the case of platelet values, but with statistically significant differences ($p<0.05$): at 6 months – 175.0±0.03 x109/l; at 12 months – 174.3±0.09 x109/l. In the case of the total number of leukocytes, the average values found were very close: at one month – 6.30±0.05 x109/l; at 6 months – 6.20±0.02 x109/l; at 12 months – 6.20±0.01 x109/l of the post-COVID-19 period.

Very significant differences were recorded in the case of hemoglobin concentrations, reaching the highest level (102.0±0.59 g/l) at 12 months. The total number of erythrocytes showed statistically significant changes and was characterized by mean values of 3.10±0.04 x1012/l at 6 months and 3.00±0.02 x1012/l at 12 months of the post-COVID-19 period. Data from the specialized literature that were obtained in patients with COVID-19 showed a significant decrease in lymphocytes, monocytes, eosinophils, hemoglobin and platelets. The lower hemoglobin level in severe cases of COVID-19 could be caused by underlying medical conditions, malnutrition, or coagulation abnormalities. Coagulation abnormality is also associated with a low platelet count. The erythrocyte sedimentation rate also showed statistically significant values ($p<0.05$) at 6 months – 25.00±0.21 mm/hour and 12 months – 22.00±0.19 mm/hour, compared to the first month of the post-COVID-19 period (26.00±0.39 mm/hour). The mean values of eosinophils and lymphocytes were devoid of statistical significance, but which tended to decrease at 12 months. According to literature data, their increased level could play an important role in the recovery of patients with mild forms of COVID-19 [16].

4.6. Dynamics of immunological indices in subjects with echo-morphological changes of the thyroid gland in the post-COVID-19 period.

In the subjects examined in the post-COVID-19 period, all classes of immunoglobulins increased compared to the first month after COVID-19. Thus, compared to the first month, IgM increased truthfully by 33.3% at 6 months and by 52.4% at 12 months; IgG increased statistically significantly by 9.9% at 6 months and 5.8% at 12 months and IgA increased by 12.8% at 6 months and 27.9% at 12 months. Lower levels of IgG have been shown to be associated with a lower amount of lymphocytes in patients with COVID-19 disease [3, 25]. Knowing that the thyroid function also includes the function of increasing immunity, the results obtained from the research carried out, offer the possibility of specifying the diagnosis and improving the treatment of complications in subjects with thyroid gland conditions in the post-COVID-19 period.

4.7. Dynamics of indicators of lipid peroxidation and the antioxidant system in subjects with eco-morphological changes of the thyroid gland in the post-COVID-19 period.

The study carried out estimated the value of the concentration serum content of the oxidative stress indices which allowed to establish a stability of the lipid hydroperoxide indices in all post-COVID-19 periods. The final product of POL, malonic dialdehyde also showed no changes, as well as enzymes of antioxidant protection (ceruloplasmin, catalase, glutathione peroxidase, superoxide dismutase and total antioxidant activity). Changes in these indicators testify to the fact that the factors of the antioxidant defense system actively participate in the

mechanisms of innate immunity, and their insufficiency can lead to extremely negative consequences during SARS CoV-2 infection. There is also evidence of a significant decrease in viral titers under the action of antioxidant enzymes. Superoxide dismutase, the main antioxidant enzyme that inactivates the superoxide radical, and catalase, which inactivates hydrogen hydroperoxide, have similar properties [20].

4.8. Psychophysiological peculiarities in the post-COVID-19 period in subjects with echo-morphological changes of the thyroid gland.

The majority of subjects presented with sleep disturbances, predominantly difficulty falling asleep at 1 month post-COVID-19 (31.1%), 6 months (24.9%) and 12 months (18.1%) in the post-COVID period -19. Frequent awakenings were observed in 27.8% of subjects at 1 month, 24.9% of subjects at 6 months, and 14.9% at 12 months. Fatigue upon waking was reported by 26.95% of the subjects at one month, 17.8% at 6 months and 8.9% of them at 12 months. Inadequate changes were observed in the nightmare domain – in 3.9% of subjects at 1 month, 5.8% at 6 months and 1.8% at 12 months.

Psychodiagnostic assessment of subjects in the post-COVID-19 period (Hamilton test). Euthymic state was determined in 389 subjects, which during the periods 1-12 months post-COVID-19 had a decreasing trend. Mild depression had a differentiated trend at 1 month in 22.8% of subjects, at 6 months with an increase (25.3%) and at 12 months it decreases in 14.9% of subjects. Moderate depression was attested at 1 month post-COVID-19 in 7.9%, at 6 months at 22.6%, at 12 months at 4.9% of subjects in the post-COVID-19 period. Significant depression was reported at 1 month in 2.9%, at 6 months in 6.6% subjects, and at 12 months in 4.7% subjects in the post-COVID-19 period. Assessing the degree of anxiety in subjects with eco-morphological changes of the thyroid gland in the post-COVID-19 period through the Spilberger test. The research demonstrated (Figure 3.4.) that the level of anxiety in the examined subjects had different trends, both at low, moderate and high levels. Low level of anxiety was appreciated at 1 month in 55.8%, at 6 months at 59.1%, at 12 months at 47.5% of the subjects examined in the post-COVID-19 period. Moderate level of anxiety was evident at 1 month in 34.8% of subjects, at 6 months in 30.2%, and at 12 months in 24.5% of subjects in the post-COVID-19 period. High level of anxiety was demonstrated in 7.9% of subjects examined at 1 month post-COVID-19, 7.3% of subjects examined at 6 months, and 6.0% of subjects examined at 12 months post - COVID-19. The exploration of the "Accentuated Personality" proves that the subjects of the study group fall within the "normal limits", the average of the accentuations for each individual subject being below the critical percentage level of 75%, $p<0.05$. It is observed that there are personality traits that can

exceed the level of average accentuation, but in the case of each subject, they are "compensated" in various forms and harmoniously integrated into the overall structure of the personality.

4.9. Pathological changes of internal organs captured by ultrasound in subjects with thyroid gland conditions post-COVID-19.

Abdominal organ disorders have also been detected in people with thyroid gland conditions post-COVID-19. Echoscopically, changes are evident in the internal organs: liver, pancreas, kidneys and genital organs (Figure 4.4.).

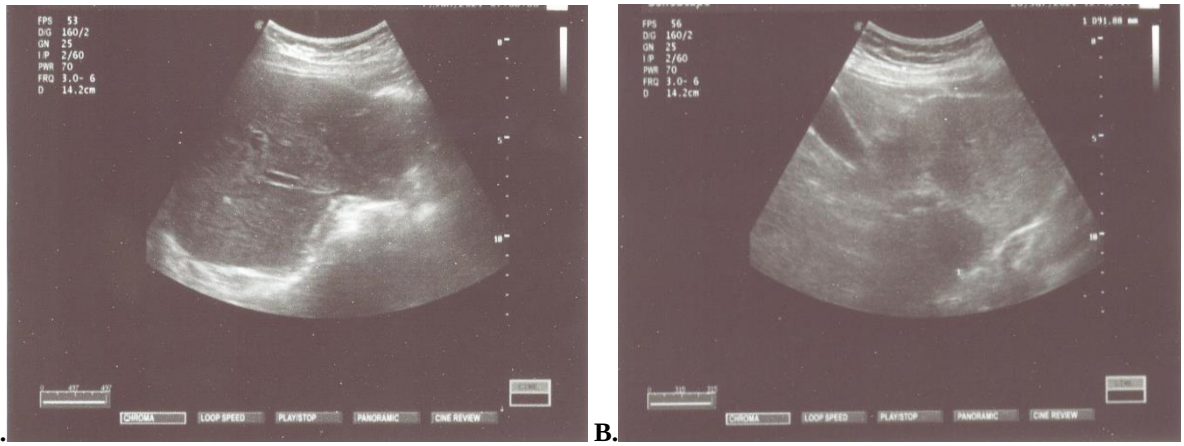


Fig. 4.4. Liver echo-morphological changes (after 1 month) (A) and (after 6 months) (B) in post-COVID-19 subjects *(original)*

As a result of the ultrasonographic investigation, 6 months post-Covid-19, the ultrasound picture diminishes, the hypoechoic areas shrink, and some disappear (Figure 4.5.). At 12 months of the post-COVID-19 period, the hypoechoic areas are weakly highlighted (Figure 4.5.).

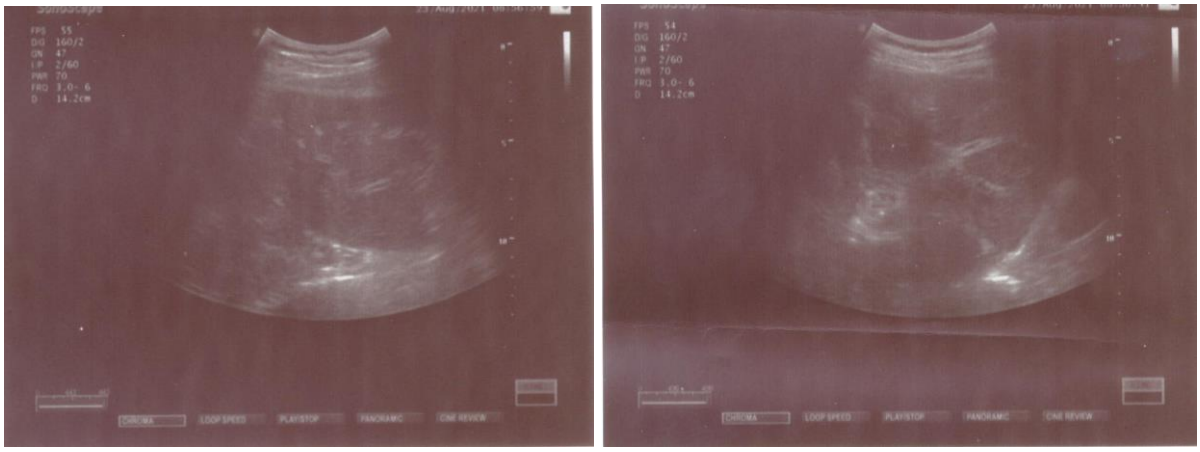


Fig. 4.5. Echomorphological changes of the liver post-COVID-19 (after 12 months) *(original)*

The echoscopic pancreas is sometimes enlarged in size, with an inhomogeneous structure, characteristic for acuteness. Echoscopic changes of the spleen are rarely found, but it can be enlarged in size and homogeneous in structure. As a result of the ultrasonographic investigations

of the kidneys, they are slightly increased in size. The pyelocalyceal area is affected in most cases "with furrows". An accentuated, thickened drawing with calyx dilations, sometimes also dilatations of the pelvis (hydronephrosis) is attested (Figure 4.6.).

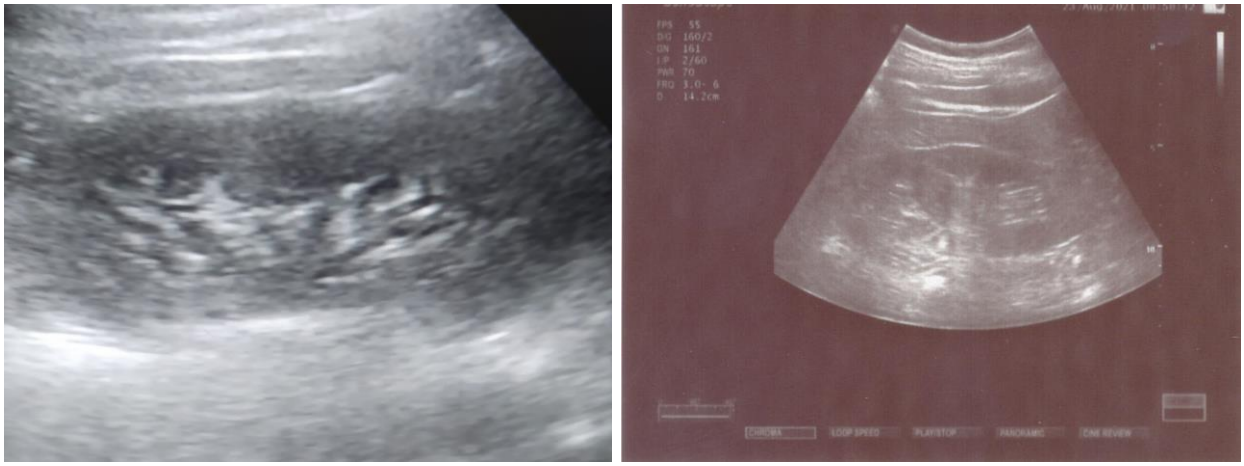


Fig. 4.6. Echo-morphological changes of kidneys post-COVID-19 *(original)*

Urine analyzes are characterized by a large number of leukocytes, rarely erythrocytes. In the post-COVID-19 period, prostate damage was also detected in men, being a mild hyperplasia, and in women, irregularities in the menstrual cycle were noted. Lung conditions were also detected by ultrasound examination of the pleural spaces, fluid collections in the pleural spaces.

4.10. Thyroid gland disorders and osteoporosis.

4.10.1. Correlation of thyroid gland conditions with osteoporosis in subjects in the pre-COVID-19 period.

According to the study carried out, from 25 to 45 years the normal bone structure was established in 12 subjects, who also had normal echo-morphological aspect of GT. Of 18 subjects, who had mild hyperplasia of the thyroid gland, 8 subjects were found to have grade I osteoporosis, and the rest showed no signs of osteoporosis. The result of the investigations confirmed the fact that osteoporotic disease is closely correlated with the function and diseases of the thyroid gland even after suffering from the COVID-19 infection. As a result of the condition of the GT and the immune system, the production of calcitonin decreases, resulting in diseases of the bone skeleton, such as osteoporosis. These conditions were also detected in subjects examined with post-COVID-19 thyroid conditions.

4.10.2. Correlation of thyroid gland conditions with osteoporosis in post-COVID-19 subjects.

Subject investigations have determined a correlation between thyroid gland conditions and osteoporosis. Research has shown that 86% of subjects with GT diseases have osteoporosis. We

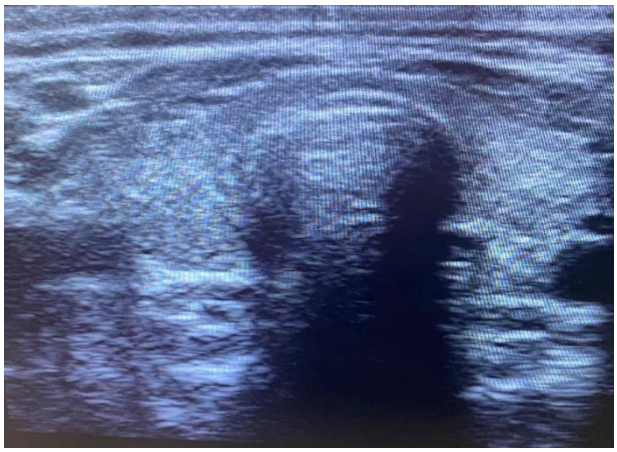
found that among patients with GT diseases, especially women suffer from varying degrees of osteoporosis. And vice versa, patients with osteoporosis have thyroid diseases.

4.11. Biological effects of phytotherapeutic dietary supplement "X" on thyroid gland function.

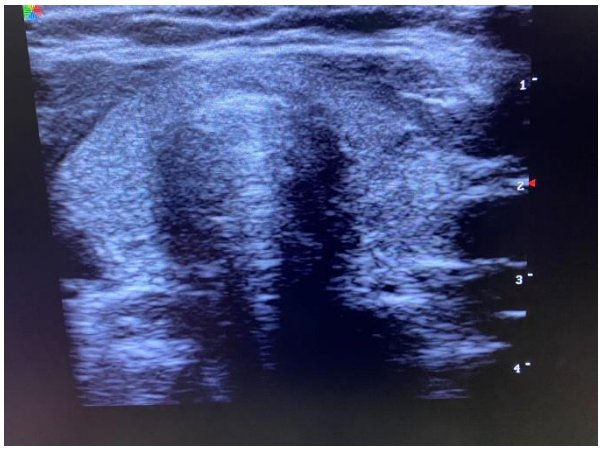
The post-COVID-19 sequelae require treatment to improve the condition of GT. For this purpose, a food supplement was developed that requires the rehabilitation of GT and the body in the post-COVID-19 period. The composition of the developed phytopreparation is based on phytotherapeutic ingredients, which can be delivered to people without a prescription, significantly shortens the recovery period and does not cause adverse reactions. Given the fact that subjects infected with SARS CoV-2 suffer from a series of associated pathologies, these factors become paramount in the establishment of the euthyroid state. The preparation reduces and stops the inflammation process, the fibrosis process. GT adapts and rehabilitates faster. As a result, the other processes in the body are also regulated. Following the use of this supplement, its biological effect was highlighted, by initiating some observational studies, which included 36 subjects in the post-COVID-19 period - at one month, at 6 months and at 12 months. The supplement was administered to the research groups 2 capsules per bone with a sufficient amount of liquid (150-200 ml of water) 3 times a day 15 minutes before meals. The analyzes were taken consecutively over one month, 6 months and 12 months of the post-COVID-19 period.

Administration for 15 days of phytotherapeutic supplement "X" demonstrated a biological effect of stimulating and readapting GT function. The beneficial result of the preparation is due to the successful selection of the quantitative and qualitative components that manifest a synergism and produce a net effect superior to their action taken separately. The concentrations of T3, T4 and TSH hormones returned to the limits of established physiological norms in all age groups. T3 level: established norm – 2.20±0.81, in the post-COVID-19 period – 1.10±0.17 and after administration of the "X" supplement was 2.30±0.42 nmol/L ($p<0.05$); T4 concentration: established norm – 108.30±20.10, in the post-COVID-19 period – 50.51±1.10, and after administration of the "X" supplement – 110.20±11.40 nmol/L ($p <0.05$); TSH value: established norm – 2.40±0.30, in the post-COVID-19 period – 11.60±0.70 and after administration of the "X" supplement – 2.40±0.10 nmol/L ($p< 0.05$).

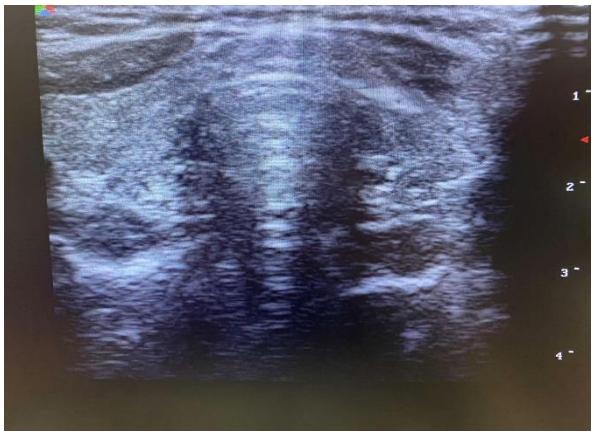
Following the administration of the remedy, a considerable attenuation of the thyroid tissue was attested (Figure 4.7.). Eco-morphologically, a decrease in the dimensions of the GT is attested, as well as the improvement of the structure of the thyroid tissue by the disappearance of the edema and by the reduction of the fibrosis process.



a) until the administration of the preparation



b) after one month of administration of the preparation



c) after 6 months of administration of the preparation

d) after 12 months of administration of the preparation

Fig. 4.7. Eco-morphology of the thyroid gland after administration of phytotherapeutic dietary supplement "X" (original)

GENERAL CONCLUSIONS

1. The action of COVID-19 on the hormonal and eco-morphological status of the thyroid gland was manifested not only as an infectious agent, but after its awareness as a factor of great danger to society and as a psychogenic factor.

2. The evaluation of the function of the thyroid gland in the post-COVID-19 period by dynamically determining the serum levels of T3, T4, AT-TG and TSH showed the presence of hyperthyroidism status at the 1-month interval, which was attenuated at the 6-month interval and went into a hypothyroid status after 12 months. The latter was manifested by the gender-independent significant decrease of T3 and T4 on average by 50-70% and the elevation of TSH up to 4.8 times [Chap. 4, subchapter 4.1., pp. 98-99].

3. The size of the thyroid gland in the post-COVID-19 period had an intelligible dynamic with its functional status. Thus, the volume of the gland in women increased at month 1 from 17.50±0.20 to 18.90±0.10 mm3, followed by a significant attested decline at month 12 -16.80±0.30 mm3 . In men, a significant change was also established after 12 months: from 21.50±0.18 mm3 it increased to 22.80±0.23 mm3 and then decreased to 21.30±0.22 mm3. Age variations were not found in both groups [Chap. 4, subchapter 4.2., p. 105].

4. Post-COVID damage to the thyroid gland excelled by significantly reducing total proteins and the prothrombotic index by up to 12% at 12 months, reflecting compromised liver function. The index of the thymol sample, the fibrosis marker, increased by 20% after 12 months and correlates authentically with the echocardiographic changes of gland sclerosing imminent in this period [Chap. 4, subchapter 4.4., pp. 109-110]. Remarkably, oxidative stress was not activated during the entire surveillance period given the statistically insignificant discrepancy of the main markers (lipid hydroperoxides, malonic dialdehyde, ceruloplasmin, catalase, glutathione peroxidase, superoxide dismutase and total antioxidant activity) [Chap. 4, subchapter 4.7., pp. 114-115].

5. The hematological changes characteristic of the post-COVID-19 period are imposed by the significant reduction of hemoglobin, erythrocytes and platelets after 1 month, and although these indices have a tendency to increase dynamically, they do not return to normal values even after 12 months. The VSH is in decline during the surveillance period (26-25-20 mm/hour), but remains significantly increased compared to the norm, a fact that indicates a sustainable inflammatory response [Chap. 4, subchapter 4.5., pp. 110-111]. The plasma levels of IgM, IgG and IgA reduced after 1 month increased in dynamics and at the distance of 12 months they reached the reference values [Chap. 4, subchapter 4.6., pp. 112-113].

6. The psychodynamic evaluation of the researched subjects in the post-COVID-19 period revealed euthymic state, anxiety, mild depression, moderate and significant depression in all three study periods (one month, 6 and 12 months). In the post-COVID-19 period, most subjects (70.5%) showed various psychophysiological peculiarities: dyssomnias at all research stages – at one month, 6 and 12 months, characterized by difficulty falling asleep (31.1%; 24.9%; 18.1%), frequent awakening (27.8%; 24.9; 14.9%), fatigue upon awakening (26.9%; 17.8%; 8.9%), dreams ugly (3.9%; 5.8%; 1.8%) [Chap. 4, subchapter 4.8., pp. 116-118].

7. Administration per os for 15 days of the phytotherapeutic dietary supplement "X" developed and patented by the author demonstrated a conclusive biological effect of improving the recovery of the morpho-functional status of the thyroid gland during the 12-month post-COVID period. Thus, the circulating levels of the hormones T3, T4, TSH and AT-TG returned to

the limits of physiological norms established in all age groups, and the size and volume of the thyroid gland marked a more moderate decline over the period of 6-12 months [Chap. 4, subchapter 4.11., p. 133-135].

PRACTICAL RECOMMENDATIONS

1. The impact of Sars-Cov-2 on the thyroid gland is conclusive, causing at a distance of 12 months the fibrosis of the gland and the establishment of a hypothyroid status, so the dynamic evaluation of circulating hormone levels and ultrasound indices is important in early prediction and optimization of therapy post-covid.

2. Phytotherapeutic dietary supplement "X" rich in iodine is recommended to be used in the rehabilitation of thyroid gland function in the post-COVID-19 period, as its oral administration for 15 days determines the normalization of circulating hormone levels (T3, T4, TSH) and reducing the degree of fibrosis of the gland at the distance of 12 months.

3. The psychophysiological, immunological, biochemical, hematological peculiarities, of carbohydrate, lipid and protein metabolism, of thyroid hormones and the eco-morphological pattern of the thyroid gland in the post-COVID-19 period, are recommended to be used as conceptual and holistic benchmarks in the university training process in physiology, endocrinology, physiopathology and ultrasonography at the State University of Medicine and Pharmacy "N. Testemițanu" and the State University of Moldova.

BIBLIOGRAPHY

1. BABSCHI, E.B., ZUBCOV A.A., KOSIȚKI G.I., HODOROV B.I. Fiziologia omului: Manual pentru studenții institutelor de medicină. Chişinău: Lumina, 1991, 624 p. ISBN 5-372-00760-5.

2. BADEA, R.I., DUDEA, S.M., MIRCEA, P.A., ZDRENGHEA, D. Tratat de ultrasonografie clinică. București: Editura Medicală, 2014, Vol. II, 460 p.

3. **CEBOTARI, A.** Dinamica imunoglobulinelor, aminoacizilor imunoactivi și a glutationului la subiecții cu schimbări eco-morfologice ale glandei tiroide în perioada post-COVID-19. Buletinul Academiei de Științe a Moldovei. Științele vieții. 2021, nr. 1 (343), 44-49. doi: 10.52388/1857-064X.2021.1.06.

4. **CEBOTARI, A.** Dinamica indicilor biochimici și hematologici la subiecții cu schimbări eco-morfologice ale glandei tiroide în perioada post-COVID-19. În: Materialele Conferinței științifice internaționale „Sănătatea, medicina și bioetica în societatea contemporană: studii inter și pluridisciplinare”, 29-30 octombrie 2021, ediția a IV-a. Chișinău: Print Caro, 2021, p. 363-368. ISBN 978-9975-56-935-4.

5. **CEBOTARI, A.** Fiziologia și ecografia glandei tiroide, paratiroide și salivare. Chișinău: S.n., Ediția a II-a, 2021, 96 p. ISBN 978-9975-87-857-9.

6. FURDUI, T., VUDU, Gr. Perioadele vârstei omului după maturizare. Zilele Univ. de Medicină şi Farmacie „N. Testemiţanu”. Materialele conf. şt. an. a colab. și studenţilor., Chişinău, 1998, p. 71. – 16

7. HĂULICĂ, I. Fiziologia umană. București: Editura Medicală, 2007, 278 p.

8. БАБАК, О.Я. Глутатион в норме и при патологии: биологическая роль и возможности клинического применения. Здоровье Украины. 2015, № 1, 32-37.

9. ПОЛОНИКОВ, А. Эндогенная недостаточность глутатиона как наиболее вероятная причина серьезных манифестаций и смерти пациентов с COVID-19. Disponibil: https://stopcovid19.com.ru/671-endogenous-deficiency-of-glutathione-as-cause-death-covid19/ (Accesat la 12.09.2020).

10. CARON, P. Thyroid disorders and SARS-CoV-2 infection: From pathophysiological mechanism to patient management. Ann Endocrinol (Paris). 2020, 81(5), 507-510. doi: 10.1016/j.

11. CHEN, W., ZHANG, Q., WU, Y., et al. Shift of reference values for thyroid volume by ultrasound in 8- to 13-year-olds with sufficient iodine intake in China. Thyroid. 2019, 29(3), 405-411. doi: 10.1089/thy.2018.0412.

12. CHEN, W. et al. Potential interaction between SARS-CoV-2 and thyroid: a review. Endocrinology. 2021, 162(3), bqab004. doi: 10.1210/endocr/bqab004.

13. DALANGIN, R., KIM, A., CAMPBELL, R.E. The role of amino acids in neurotransmission and fluorescent tools for their detection. Int J Mol Sci. 2020, 21(17), 6197. doi: 10.3390/ijms21176197.

14. DRUCKER, D. Endocrine targets related to COVID-19 infection. Endocrine Abstracts. 2020, 70, CS1.1. doi: 10.1530/endoabs.70.CS1.1

15. GHEZZI, P. Role of glutathione in immunity and inflammation in the lung. Int J Gen Med. 2011, 4, 105-113.

16. HARIYANTO, T.I., KURNIAWAN, A. Thyroid disease is associated with severe coronavirus disease 2019 (COVID-19) infection. Diabetes Metab Syndr. 2020, 14 (5), 1429-1430.

17. HE, B., WANG, J., WANG, Y. et al. The Metabolic Changes and Immune Profiles in Patients With COVID-19. Front Immunol. 2020, 11, 2075. doi: 10.3389/fimmu.2020.02075. eCollection 2020.

18. IVARSSON, S.A., PERSSON, P.H., ERICSSON, U.B. Thyroid gland volume as measured by ultrasonography in healthy children and adolescents in noniodine-deficient area. Acta Paediatrica Scandinavica. 1989, 78, 633-634.

19. KHOO, B., TAN, T., CLARKE, S.A. et al. Thyroid function before, during, and after COVID-19. J Clin Endocrinol Metab. 2021, 106(2), e803-e811. doi: 10.1210/clinem/dgaa830.

20. KOMARAVELLI, N., CASOLA, A. Respiratory Viral Infections and Subversion of Cellular Antioxidant Defenses. J Pharmacogenomics Pharmacoproteomics. 2014, 5(4), 1000141. doi: 10.4172/2153-0645.1000141.

21. LANIA, A. et al. Thyrotoxicosis in patients with COVID-19: the THYRCOV study. Eur J Endocrinol. 2020, 183 (4), 381-387.

22. RUGGERI, R.M. et al. Influence of Dietary Habits on Oxidative Stress Markers in Hashimoto's Thyroiditis. Thyroid. 2021, 31(1), 96-105. doi: 10.1089/thy.2020.0299.

23. SPEER, G., SOMOGYI, P. Thyroid complications of SARS and coronavirus disease 2019 (COVID-19). Endocr J. 2021, 68(2), 129-136. doi: 10.1507/endocrj.EJ20-0443.

24. WU, H., ZHU, H., YUAN, C. et al. Clinical and Immune Features of Hospitalized Pediatric Patients With Coronavirus Disease 2019 (COVID-19) in Wuhan, China. JAMA Netw Open. 2020, 3(6), e2010895. doi: 10.1001/jamanetworkopen.2020.10895.

25. ZHAO, J, YUAN, Q, WANG, H. et al. Antibody responses to SARS-CoV-2 in patients with novel coronavirus disease 2019. Clin Infect Dis. 2020, 71(16), 2027-2034. doi: 10.1093/cid/ciaa344.

LIST OF PUBLISHED WORKS ON THE THEME OF THE THESIS

1. Monographs

1. **CEBOTARI, A.** *Ecografia glandei tiroide, paratiroide și salivare*. Chișinău: Centru editorial „PRESA”, 1996, 231 p. ISBN 5-85268-249-7.

2. **CEBOTARI, A.** *Fiziologia și ecografia glandei tiroide, paratiroide și salivare*. Chișinău: S.n., Ediția a II-a, 2021, 96 p. ISBN 978-9975-87-857-9.

2. Articles in scientific journals

2.2. in journals from the Web of Science and SCOPUS databases.

3. **CEBOTARI, A.** Physiological and echo-morphological aspects of the thyroid gland in the pre- and post-COVID-19 period. *Int. J. Adv. Res.* 2021, 9(08), 425-433. Doi:10.21474/IJAR01/13284. ISSN: 2320-5407. (Impact Factor: 7,33)

2.3. in magazines from the National Register of professional magazines, Category B.

4. MEREUȚĂ, I., FEDAȘ, V., TOMȘA, A., **CEBOTARI, A.** Sindromul metabolic și alte comorbidități în structura mortalității prin COVID-19 în Republica Moldova (martie-decembrie 2020). *Buletinul Academiei de Științe a Moldovei. Științe medicale.* 2021, nr. 2 (70), 40-45. ISSN 1857-0011.

5. МЕРЕУЦЭ, И.Е., СТРУТИНСКИЙ, Ф.А., БОДРУГ, Н.И., ПОЛЯКОВА, Л.Д., КАРАУШ, В.Ф., **ЧЕБОТАРЬ, А.Я.** Особенности метаболизма глутатиона при COVID-19. *Buletinul Academiei de Ştiinţe a Moldovei. Ştiinţe medicale.* 2021, nr. 2 (70), 137-142. ISSN 1857-0011.

6. **CEBOTARI, A.** Dinamica imunoglobulinelor, aminoacizilor imunoactivi și a glutationului la subiecții cu schimbări eco-morfologice ale glandei tiroide în perioada post-COVID-19. *Buletinul Academiei de Științe a Moldovei. Științele vieții.* 2021, nr. 1 (343), 44-49. doi: 10.52388/1857-064X.2021.1.06. ISSN 1857-064X. (Cat. B)

3. Articles in scientific collections

3.2. in the proceedings of international scientific conferences (Republic of Moldova)

7. **CEBOTARI, A.** Particularități psihofiziologice în perioada post-COVID-19 la subiecții cu schimbări eco-morfologice ale glandei tiroide. În: Materialele Conferinței Științifice cu participare Internaţională „*Tradiţie şi inovare în cercetarea ştiinţifică*”, 8 octombrie 2021, ediţia a X-a, vol. 1. Bălți: CEU US, 2022, p. 179-183. ISBN 978-9975-50-270-2. ISBN 978-9975-50-271-9 (vol.1).

8. **CEBOTARI, A.** Dinamica indicilor biochimici și hematologici la subiecții cu schimbări eco-morfologice ale glandei tiroide în perioada post-COVID-19. În: Materialele Conferinței științifice internaționale „*Sănătatea, medicina și bioetica în societatea contemporană: studii inter și pluridisciplinare*”, 29-30 octombrie 2021, ediția a IV-a. Chișinău: Print Caro, 2021, p. 363-368. ISBN 978-9975-56-935-4.

9. **CEBOTARI, A.** Schimbari fiziologice si eco-morfologice ale colecistului și rinichilor la subiecții cu afecțiuni ale glandei tiroide. În: Materialele Conferinței științifice internaționale „*Sănătatea, medicina și bioetica în societatea contemporană: studii inter și pluridisciplinare*”, 29-30 octombrie 2021, ediția a IV-a. Chișinău: Print Caro, 2021, p. 375-377. ISBN 978-9975-56-935-4.

3.3. in the proceedings of national scientific conferences with international participation

10. **CEBOTARI, A.** Ultrasonografia glandei tiroide – una din metodele de profilaxie în depistarea osteoporozei. În: Culegerea de lucrări ale Conferinței științifice naționale cu participare internațională dedicată aniversării a 75-a a Universității de Stat din Moldova „*Integrare prin cercetare și inovare*”. Chișinău: CEP USM, 2021, p. 28-30. ISBN 978-9975-152-48-8. ISBN 978-9975-158-60-2.

11. MEREUȚĂ, I., **CEBOTARI, A.** Dinamica indicatorilor peroxidării lipidice și a sistemului antioxidant la subiecții cu schimbări eco-morfologice ale glandei tiroide în perioada post-COVID-19. În: Culegerea de lucrări ale Conferinței științifice naționale cu participare internațională

dedicată aniversării a 75-a a Universității de Stat din Moldova „*Integrare prin cercetare și inovare*”. Chișinău: CEP USM, 2021, p. 41-43. ISBN 978-9975-152-48-8. ISBN 978-9975-158-60-2.

4. Theses in scientific collections

4.3. in the proceedings of national scientific conferences with international participation

12. MEREUȚĂ, I., TOMȘA, A., BACIU, A., **CEBOTARI, A.**, FEDAȘ, V. Boala coronavirus și factorii cu risc metabolic crescut – probleme și soluții. In: *Biotehnologii moderne – soluții pentru provocările lumii contemporane*: Lucrările Simpozionului științific național cu participare internațională, 20-21 mai, 2021, Chișinău, p. 71. Doi: 10.52757/imb21.037. ISBN 978-9975-3498-7-1

4.5. in other collections of scientific works published abroad

13. **CEBOTARI, A.**, BAIRAC, V., GAVRILIUC, L., ANESTIADI, Z., CIOCÎRLAN, I. Ultrasonographic diagnosis criteria in thyroid diseases. In: *Diagnostic și tratament în patologia tiroidiană. Osteoporoza*: Lucrările Simpozionului național de endocrinologie și al XII-lea Simpozion de endocrinologie clinică, 5-6 mai, 1995, Iași, p. 271-273.

ADNOTARE

Cebotari Anghela, „Particularitățile fiziologice și eco-morfologice ale glandei tiroide în perioada post-COVID-19”. Teză de doctor în științe biologice, Chișinău, 2023.

Structura tezei: introducere, patru capitole, concluzii generale şi recomandări practice, bibliografie din 273 de titluri, 15 anexe, 142 de pagini de text de bază, 52 figuri, 29 tabele. Rezultatele obţinute sunt publicate în 13 de lucrări ştiinţifice.

Cuvinte-cheie: glanda tiroidă, fiziologie, infecția SARS CoV-2, maladia COVID-19, particularități fiziologice, particularități eco-morfologice, perioadă pre- și post-COVID-19, hormoni tiroidieni, metabolism.

Scopul lucrării: Evaluarea particularităților funcționale și eco-morfologice ale glandei tiroide la pacienții infectați cu SARS CoV-2 în perioada post-COVID-19, precum și a modalității de favorizare a reabilitării fiziologice.

Obiectivele cercetării: 1) Evaluarea statusului hormonal al glandei tiroide în perioada pre- și post-COVID-19. 2) Evidențierea eco-morfologică a glandei tiroide în perioada pre- și post COVID-19. 3) Estimarea unor indici metabolici ce reflectă pericolul dereglării metabolismului, stresului oxidativ și markerului de fibroză (indicele probei cu timol) la pacienții cu afecțiunea post-COVID a glandei tiroide. 4) Studiul dinamicii modificării hematologice în perioada post-COVID-19 la pacienții cu afecțiunea post-COVID a glandei tiroide. 5) Estimarea statusului psihofiziologic al pacienților cu afecțiuni post-COVID-19 ale glandei tiroide. 6) Elaborarea unui supliment alimentar fitoterapeutic, ce ar favoriza reabilitarea fiziologică a glandei tiroide în perioada post-COVID-19.

Noutatea și originalitatea ştiinţifică: A fost evaluat statusul hormonal și eco-morfologic pre-COVID al glandei tiroide pe un eșantion de 5705 de persoane ce a permis de a demonstra nu numai dinamica hormonală și eco-morfologică a glandei tiroide în condițiile contemporane de fiecare zi, dar și de a stabili de prima dată dereglarea funcției fiziologice și schimbările eco-morfologice ale glandei tiroide, cauzată de infecția SARS CoV-2. Și mai mult, studiul complex fiziologic, eco-morfologic, biochimic, hematologic și psihofiziologic a demonstrat că infecția SARS CoV-2 influențează și asupra altor organe și sisteme. În premieră a fost elaborat și cercetat efectul suplimentului alimentar fitoterapeutic „X” bogat în iod patentat de autor asupra restabilirii funcționale și morfologice a glandei tiroide pe perioada post-COVID de 12 luni.

Rezultatul obținut, care contribuie la soluționarea unei probleme științifice importante. Influența COVID-19 asupra organismului, recuperarea stării fiziologice și eco-morfologice în perioada post COVID-19, constă în demonstrarea modificărilor fiziologice și eco-morfologice la subiecții cu consecințe COVID-19 care s-au reflectat și asupra glandei tiroide în perioada post-COVID-19, precum și elaborarea unui supliment alimentar în scopul readaptării fiziologice și eco-morfologice a glandei tiroide și a metabolismului. Schimbările eco-morfologice, fibroza țesutului glandular și hipofuncția glandei tiroide în perioada post-COVID-19, pot fi stopate și îmbunătățite de către acțiunea fitopreparatului elaborat.

Semnificaţia teoretică constă în obținerea noilor date despre influența infecției SARS CoV-2 asupra statusului hormonal și eco-morfologic a glandei tiroide și a altor organe în perioada post-COVID-19 la o lună, 6 și 12 luni, ce prezintă un suport suficient în dezvăluirea mecanismelor dereglării funcției și structurii glandei tirode.

Valoarea aplicativă a lucrării constă în realizarea unui studiu, ce a permis de a aduce dovezi semnificative practice a participării glandei tiroide în procesul patologic cauzat de COVID-19 și elaborarea unui supliment alimentar, ce recuperează starea fiziologică și eco-morfologică în perioada post-COVID-19.

Implementarea rezultatelor ştiinţifice: Rezultatele cercetărilor se implementează în procesul de cercetare, în programele de readaptare, reabilitare fiziologică și metabolică post-COVID-19, în procesul de diagnosticare ultrasonografică, în entitățile științifice – Institutul de Fiziologie și Sanocreatologie, Universitatea de Stat din Moldova, Universitatea de Stat de Medicină și Farmacie „N. Testemițanu”, în Institutul Oncologic, în Universitatea „Ioan Cuza” din Iași, în Centrul Medical de diagnostic și tratament ambulatoriu al Ministerului Justiției din București, în cabinetele consultative endocrinologice publice și private.

АННОТАЦИЯ

Чеботарь Ангела, «Физиологические и экоморфологические особенности щитовидной железы в период после COVID-19». Докторская диссертация по биологическим наукам, Кишинев, 2023.

Структура диссертации: введение, четыре главы, общие выводы и практические рекомендации, библиография из 273 наименований, 15 приложений, 142 страниц основного текста, 52 рисунка, 29 таблиц. Полученные результаты опубликованы в 13 научных статьях.

Ключевые слова: щитовидная железа, физиология, инфекция SARS CoV-2, заболевание COVID-19, физиологические особенности, эколого-морфологические особенности, период до и пост-COVID-19, гормоны щитовидной железы, метаболизм.

Цель работы: Оценка функциональных и эко-морфологических особенностей щитовидной железы в посткоронавирусном периоде, а также пути оптимизации физиологической реабилитации.

Задачи исследования: 1) Оценка физиологического статуса щитовидной железы в до- и пост-COVID-19 периоде. 2) Экоморфологическое исследование щитовидной железы в период до и пост-COVID-19. 3) Исследование изменений показателей метаболизма, окислительного стресса и маркера фиброза (индекс тимолового теста) у пациентов с постковидным заболеванием щитовидной железы. 4) Оценка гематологических особенностей, присущих пост-COVID-19 периоду у пациентов с пост-COVID-заболеванием щитовидной железы. 5) Оценка психофизиологического статуса пациентов с посткоронавирусными состояниями щитовидной железы. 6) Обоснование влияния фитотерапевтической пищевой добавки «X» на физиологическую реабилитацию щитовидной железы в посткоронавирусный период.

Научная новизна и оригинальность: На выборке из 5705 человек проведена оценка физиологического и эко-морфологического статуса щитовидной железы до-COVID с целью выделения группы здоровых лиц, у которых в пост-COVID-период наблюдалась опасность для щитовидной железы, а также другая часть — установить морфологические закономерности изменения желез до COVID, чтобы выявить экоморфологические особенности после COVID. В постковидный период было проведено комплексное физиологическое, экоморфологическое, биохимическое, иммунологическое, гематологическое, метаболическое и психофизиологическое исследование с целью определения особенностей изменений гомеостаза, неизбежных при воздействии Sars-Cov-2 на щитовидную железу. здоровые люди до COVID. Впервые исследовано влияние запатентованной автором фитотерапевтической БАД «X», богатой йодом, на функциональное и морфологическое восстановление щитовидной железы в течение 12-месячного постковидного периода.

Полученный результат, способствующий решению важной научной задачи, заключается в определении физиологических и экоморфологических изменений у лиц с изменениями щитовидной железы в пред- и пост-COVID-19 периоде и развитии некоторых механизмы и методы физиологической перестройки метаболизма щитовидной железы в эпоху пост-COVID-19. Экоморфологические изменения, фиброз железистой ткани и гипофункция щитовидной железы в посткоронавирусном периоде могут быть замещены действием фитопрепарата «X».

Теоретическая значимость состоит в определении функциональности щитовидной железы в динамике в посткоронавирусном периоде и определении физиологических и эко-морфологических изменений в посткоронавирусном периоде через один месяц, 6 месяцев и 12 месяцев.

Прикладная ценность работы заключается в получении данных о физиологических и экоморфологических изменениях щитовидной железы в посткоронавирусном периоде и изучении механизмов функциональной и метаболической активности. Результаты используются при обучении персонала, а также в процессе реадаптации и реабилитации после COVID-19.

Внедрение научных результатов: Результаты исследований внедрены в научный процесс, в программы реадаптации, физиологической и метаболической реабилитации после COVID-19, в процесс ультразвуковой диагностики, в научные учреждения - Институт физиологии и санократологии Государственного университета. Молдовы, Государственный медико-фармацевтический университет «Н. Тестемицану», в Онкологическом институте, в Университете «Иоан Куза» в Яссах, в государственных и частных эндокринологических кабинетах.

ANNOTATION

Cebotari Anghela, "Physiological and eco-morphological peculiarities of the thyroid gland in the post-COVID-19 period". Doctoral thesis in biological sciences, Chisinau, 2023.

Structure of the thesis: introduction, four chapters, general conclusions and practical recommendations, bibliography of 273 titles, 15 appendices, 142 pages of basic text, 52 figures, 29 tables. The obtained results are published in 13 scientific papers.

Key words: thyroid gland, physiology, SARS CoV-2 infection, COVID-19 disease, physiological features, eco-morphological features, pre- and post-COVID-19 period, thyroid hormones, metabolism.

The purpose of the work: Evaluation of the functional and eco-morphological peculiarities of the thyroid gland in the post-COVID-19 period, as well as the way to optimize physiological rehabilitation.

Research objectives: 1) Evaluation of the physiological status of the thyroid gland in the pre- and post-COVID-19 period. 2) Eco-morphological research of the thyroid gland in the pre- and post-COVID-19 period. 3) Study of changes in metabolic indices, oxidative stress and fibrosis marker (thymol test index) in patients with post-COVID thyroid gland disease. 4) Appreciation of the hematological peculiarities inherent in the post-COVID-19 period in patients with post-COVID thyroid gland disease. 5) Estimation of the psychophysiological status of patients with post-COVID-19 conditions of the thyroid gland. 6) Validation of the effect of phytotherapeutic food supplement "X" on the physiological rehabilitation of the thyroid gland in the post-COVID-19 period.

Scientific novelty and originality: The pre-COVID physiological and eco-morphological status of the thyroid gland was evaluated on a sample of 5705 people in order to identify a group of healthy subjects, who in the post-COVID period demonstrated thyroid endangerment, and on another part to establish the pre-COVID morphological patterns of gland alteration to detect the post-COVID eco-morphological peculiarities. In the post-COVID period, a complex physiological, eco-morphological, biochemical, immunological, hematological, metabolic and psychophysiological study was carried out to determine the particularities of homeostasis changes imminent to the impact of Sars-Cov-2 on the thyroid gland in healthy pre-COVID people. For the first time, the effect of the phytotherapeutic dietary supplement "X" rich in iodine patented by the author on the functional and morphological restoration of the thyroid gland during the 12-month post-COVID period was investigated.

The result obtained, which contributes to the solution of an important scientific problem, consists in the determination of physiological and eco-morphological changes in subjects with changes in the thyroid gland in the pre- and post-COVID-19 period and the development of some mechanisms and methods of physiological readjustment of the metabolism of the thyroid gland in the post-COVID-19 era. Eco-morphological changes, fibrosis of the glandular tissue and hypofunction of the thyroid gland in the post-COVID-19 period, can be substituted by the action of phytopreparation "X".

The theoretical significance consists in determining the functionality of the thyroid gland in dynamics in the post-COVID-19 period and determining the physiological and eco-morphological changes in the post-COVID-19 period at one month, 6 months and 12 months.

The applicative value of the work consists in obtaining evidence regarding the physiological and eco-morphological changes of the thyroid gland in the post-COVID-19 period and studying the mechanisms of functional and metabolic activity. The results are used in the training of staff, but also in the process of re-adaptation and rehabilitation post-COVID-19.

Implementation of the scientific results: The research results are implemented in the research process, in the readaptation, physiological and metabolic rehabilitation programs post-COVID-19, in the ultrasonographic diagnosis process, in the scientific entities - Institute of Physiology and Sanocratology, State University of Moldova, State University of Medicine and Pharmacy "N. Testemițanu", in the Oncological Institute, in the "Ioan Cuza" University in Iași, in public and private endocrinological consulting rooms.