

RESEARCH ARTICLE

PHYSIOLOGICAL AND ECHO-MORPHOLOGICAL ASPECTS OF THE THYROID GLAND IN THE PRE- AND POST-COVID-19 PERIOD

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 Manuscript Info
 Abstract

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 The properties of the response of the hormonally productive function,

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The properties of the response of the hormonally productive function, the echo-morphology of the thyroid gland and the tropic action of the adenohypophysis to the impact of SARS Sov-2 during postCOVID-19 period were revealed and described, depending on the age and gender of the patients.

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Introduction:-

The coronavirus (SARS-CoV2) is a new virus and there is no information on how this virus affects people with thyroid disease. Representatives of the British Thyroid Association and the British Thyroid Foundation claim that there is no evidence of thyroid disease association with an increased risk of viral infections in general, nor any association between thyroid disease and the severity of viral infection is there (Boelaert, K., et al., 2020). There is also no evidence that people with thyroid disease who have recently undergone radioactive iodine therapy or who have undergone surgery for benign thyroid disease have an increased risk of viral infections and therefore COVID-19 (Cebotari, A., 2021). Given the current context of the Covid-19 pandemic, most patients with various diseases have been affected, some of whom are no longer able to benefit from routine medical consultations. Among them are patients with thyroid disease, either with hypo- or hyperthyroidism. Endocrinologists in European centers have come together to write an article about the impact of Covid-19 on thyroid disease, but also thyroid disease impact on Covid-19 (Boelaert, K., et al., 2020). In the context of the Covid-19 pandemic, there was a necessity for examining the thyroid gland, specific thyroiditis. Especially since many elements of biological samples correlate much better with Covid-19 than with other manifestations of thyroid viral infections: very low sideremia, lymphopenia, very high ESR and C-reactive protein (Mereuta, I., et al, 2021; Mereuta, I.E., Strutinschi, F.A., et al., 2021). Due to thyroid destruction, hyperthyroxemia is obviously present, and this with a very high value, and consequently, the decrease of TSH. The syndrome is obviously hyperthyroidism (Mereuta, I., Fedas, V., et al., 2021). Therefore, the purpose of the research was to study the physiological and echo-morphological aspects of the thyroid gland in the pre- and post-covid-19 period.

Material and Methods:-

The research work was carried out in patients (n = 482) whose hospital charts were stored in the database of medical institutions. All of them were examined ultrasonographically during the years 1990-2002; 2018-2021 and the ecomorphology of their thyroid gland during the years 2020-2021 and which were confirmed with Covid-19 disease by specific and clinical test. Subjects included in the study underwent post-Covid-19 ultrasound examination at 1 month, 6 months and 12 months. Subjects were grouped as follows: up to 20 years (n = 12, 2.48 %); 20-30 years (n = 58, 12.03 %); 30-40 years (n = 87, 18.04 %); 40-50 years (n = 151, 31.32 %) and 50-60 years (n = 174, 36.12 %).

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Women constituted a total of 256 (53.11%), and men 226 (46.89%). Clinical and cross-morphological observations were described analytically. In order to highlight the biological effect of the remedy "Angel" on the function of the thyroid gland observational studies were initiated in patients (n = 36) during the postcovid period: 1 month, 6 months and 12 months. The remedy was administered to the research groups 20 ml diluted in 100 ml of water, tea or fruit juice 3 times a day, 30 minutes before a meal. The remedy was administered during 1-month post-Covid-19 period, 2 months, 5 months and 11 months. The analyzes were taken consecutively over 1-month, 6-months and 12-months postcovid period. Ultrasound (USG) examination of the thyroid gland was performed by the Philips EnVisor HD7XE (Philips, Germany) using a linear probe with a frequency of 7-12 MHz. The dimensions, volume, contour, echogenicity of the gland and the structure of the glandular tissue, the presence or lack of solid or cystic formations in the glandular tissue were assessed. The determination of thyroid gland hormones (T3, T4, TSH) was performed using the cobas® 6000 analyzer by the electrochemical method with electrochemiluminescence detection (ECLIA).

Results and Discussion:-

For the anatomical highlighting, the volume of the thyroid gland and the physiological effects of the hormones T3, T4, TSH were examined in dependence on age, sex, body weight in 100 subjects with informed consent: 50 women and 50 men grouped in the age categories: 20-30; 30-40; 40-50 and 50-60 years. In this way we homogenized the groups and studied the volume of the thyroid gland, the size and functions of the thyroid gland and effects of thyroid hormones. Table 1. Consists of the characteristic of thyroid gland dimensions in subjects examined according to age categories. There was a tendency to increase the size of thyroid gland in the age categories: 20-30, 30-40 and 40-50 years, and a decreasing trend in the age category: 50-60 years. This feature is specific to both thyroid gland lobes and isthmus.

Age	Dimensions thyroid	Dimensions thyroid gland / isthmus			
(years)	Women	Men			
20-30	16x12x38 mm/3mm	18x14x38 mm/4mm			
30-40	18x14x38 mm/4mm	19x15x39 mm/5mm			
40-50	18x12x37 mm/3mm	19x14x39 mm/4mm			
50-60	16x12x36 mm/2mm	18x13x37 mm/3mm			

Table 1:- Thyroid gland size characteristic in the examined subjects.

Table 2. shows the research data of the thyroid gland volume by gender. It is significant that the thyroid gland in men had an average volume of $21.5 \pm 1.12 \text{ mm}^3$, and in women: $17.5 \pm 1.08 \text{ mm}^3$, which proves a significant difference. At the same time, thyroid hormones were studied, the level of which in men proved to be lower than in women, both T3 and T4, while the amount of TSH, conversely, decreased. In men, the level of T3 hormone was 2.1 ± 0.98 , and in women: $2.22 \pm 1.04 \text{ (nmol/L)}$; the T4 level in men was 101 ± 11.8 , and in women: $128 \pm 14.9 \text{ (nmol/L)}$. The TSH level in men was 2.75 ± 1.3 and in women: $2.35 \pm 1.2 \text{ (nmol/L)}$.

Table 2:- Volume and function of the thyroid gland in subjects examined by gender.

Age	Gender	Thyroid gland		Hormones	
(years)		Volume	T3 (nmol/L)	T4 (nmol/L)	TSH (nmol/L)
		(mm^3)			
20-30	Female	21.5±1.1	2.10±0.98	101.0±11.8	2.75±1.3
30-40	Male	17.5±1.1	2.22±1.09	128.0±14.9	2.35±1.2

The volume of the thyroid gland and thyroid hormones was studied not only depending on age categories, but also by the gender. The research data presented in Table 3 has significantly shown that both the volume and function of the thyroid gland are different in different age categories. The volume of the thyroid gland manifests a growth curve with age and after 60 years the volume decreases up to 18.01 ± 0.1 cm³. In males, the indices were increased by 1.2 ± 0.3 mm³, compared to females.

Table 3:- Volume and hormones of the thyroid gland in age-dependent subjects.

Age (years) / gender	Thyroid gland	Hormones			
	Volume (mm ³)	T3 (nmol/L)	T4 (nmol/L)	TSH (nmol/L)	
20-30					
Female	17.50±0.20	2.20 ± 0.05	106.5 ± 22.8	2.30±0.06	

Male	21.50±0.18	2.14±0.01	108.3±20.1	2.40±0.30
30-40				
Female	21.60±0.18	2.30±0.19	147.8 ± 24.6	2.40±0.10
Male	23.80±0.30	2.35±0.19	$148.4{\pm}22.8$	2,50±0,03
40-50				
Female	21.10±0.10	2.30 ± 0.08	151.3±18.4	2.50 ± 0.80
Male	23.20±0.20	2.30±0.12	153.4±21.6	2.50±0.30
50-60				
Female	16.00±0.10	$1.84{\pm}0.08$	152.2±17.9	$2.50{\pm}1.40$
Male	18.00±0.10	1.96±0.12	153.4±19.4	$2.40{\pm}1.50$

The average level of thyroid hormones T3 and T4 showed elevation. The concentration of T3 hormone in men increased by 0.12 ± 0.02 (nmol/L) compared to women, and T4 hormone decreased in the group of 20-30 years, compared to 50-60 years in 106.0 ± 22.8 to 153.4 ± 21.12 (nmol/L).

Given the influence of body weight on thyroid gland volume, the thyroid gland volume depending on body weight was investigated (Table 4).

Table 4:- Thyroid gland volume depending on body weight.

Age (years)	Body weight (kg)	Thyroid gland
		Volume (mm ³)
Up to 20	41-50	15.75±0.80
20-30	51-60	18.75±0.60
30-40	61-70	22.50±0.50
40-50	71-80	26.00±0.10
50-60	81-90	29.00±0.10

The table shows the increase of thyroid gland volume depending on the age categories by 3.01 mm³. This conclusion is necessary for the anthropological correlation of the thyroid gland depending on age, weight and pathology.

Ultrasonographic examination was performed in patients included in the study in the post-Covid-19 period at 1 month, 6 months and 12 months.

Data from Fig. 1shows the echo-morphology of the normal thyroid gland. At 1 month of the post-Covid-19 period, the thyroid gland remains in pronounced edema, enlarged, characterized as diffuse hyperplasia of grade II-III, net contour, relatively homogeneous structure, but with low echogenicity, characteristic of thyroid parenchyma edema. In Fig. 2and Fig. 3edema, low echogenicity and increased vascularization are observed at this postcovidic time point.



FIG. 1:- Echo-morphology of the normal thyroid gland.



FIG. 2:- Presence of edema and hyperplasia at 1 month of the post-Covid-19 period



FIG. 3:- The presence of increased vascularization at 1 month of the post-Covid-19 period.



FIG. 4:- Presence of increased echogenicity at 6 months of the post-Covid-19 period.



FIG. 5:- Onset of 6-month sclerosis of the post-Covid-19 period.

At 12 months post-Covid-19 on the background of fibrosis, the thyroid gland shrinks, atrophy of the glandular tissue and replacement of connective tissue and fibrosis is observed (Fig. 6).



FIG. 6:- Presence of sclerofibrosis at 12 months of the post-Covid-19 period.

It should be noted that thyroid gland atrophy occurs not only in volume (Fig. 7), but also in functionality, appears the hypothyroidism clinic: weight gain, movement belts, thinking, memory disorders, concentration, asthenia, depression, sensation in the throat and suffocation, constipation, even menstrual disorders, etc. Metabolic disorder and type II diabetes occur.



FIG. 7:- Decreased thyroid gland at 12 months of the post-Covid-19 period.

Table 5:- Dynamics of thyroid gland volume in post-Covid-19 age/sex-dependent variations.					
Age (years) /	The established norm	1 month	6 months	12 months	
gender	$V (mm^3)$	$V (mm^3)$	$V (mm^3)$	$V (mm^3)$	
20-30					
Female	17.50±0.20	18.9±0,3*	17.8±0.4	16.8±0,3*	
Male	21.50±0,18	22.8±0,2*	21.9±0.3	21.3±0.2*	
30-40					
Female	21.6±0.2	22.4±0,3	21.9±0.3	21.4±21.2*	
Male	23.8±0.3	25.1±0.2	23.9±0.5	23.3±0.4*	
40-50					
Female	21.1±0.1	22.9±0.4	21.8±0.4	21.2±0.1*	
Male	23.2±0.2	24.9±0.3	23.4±0.3	23.0±0.1*	
50-60					
Female	16.0±0.1	17.6±0.3	16.4±0.4*	14.9±0.1*	
Male	18.0±0.1	19.8±0.3	18.8±0.7	18.0±0.1*	

Table 5:-	Dynamics	of thyroid g	land volume in	post-Covid-19	age/sex-dependent v	variations.

The physiological indices and the thyroid hormone level in the subjects studied during the years 1990-2002 and 2020-2021 depending on age and gender had conclusive values (Table 6, 7, and 8). At the age of 20-30 years, the concentration of T3 hormone in women is 2.20 ± 0.05 and in men: 2.14 ± 0.10 (nmol/L). Concentration of T4 hormone in women is 106.5 ± 22.8 , and in men: 108.3 ± 20.1 (nmol/L). Concentration of TSH in women is 2.30 ± 0.06 and in men: 2.40 ± 0.30 (nmol/L).

Age (years) /	The established norm	1 month	6 months	12 months
gender	(nmol/L)	(nmol/L)	(nmol/L)	(nmol/L)
20-30				
Female	2.20 ± 0.05	2.40±0.06*	2.30±0.17	1.10±0.17*
Male	2.14±0.01	2.38±0.11*	2.20±0.19	1.20±0.11*
30-40				
Female	2.30±0.19	2.39±0.17	2.37±0.04	1.20±0.14*
Male	2.35±0.19	2.40 ± 0.08	2.31±0.06	1.12±0.17*
40-50				
Female	2.30 ± 0.08	2.39±0.11	2.30±0.07	1.20±0.13*
Male	2.30±0.12	2.38±0.09	2.30±0.08	1,20±0,11*
50-60				
Female	1.84 ± 0.08	1.98 ± 0.01	1.34±0.09*	1,11±0,14*
Male	1.96±0.12	2.00±0.09	1.98 ± 0.07	1,14±0,13*

Table 6:- T3 hormone of the thyroid gland in the post-Covid-19 period.

At the age of 30-40 the level of T3 hormone in women is 2.30 ± 0.19 , and in men 2.35 ± 0.19 (nmol/L); the concentration of 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 7:- T4 hormone of the thyroid gland in the post-Covid-19 period.

Age (years)	The established	The established 1 month		12 months
/ gender	norm (nmol/L)	(nmol/L)	(nmol/L)	(nmol/L)
20-30				
Female	106.5 ± 22.8	108.4±21.6	77.3±11.9	50.3±1.3*
Male	108.3±20.1	109.0±22.4	78.4±29.3	50.5±1.1*
30-40				
Female	147.8±24.6	149.0±19.6	74.6±11.9*	52.1±1.1*
Male	148.4±22.8	150.0±17.3	79.0±18.7*	51.2±1.2*
40-50				
Female	151.3 ± 18.4	152.0±18.9	72.6±22.1*	50.4±1.8*
Male	153.4±21.6	154.6±15.3	74.8±19.3*	52.1±1.2*
50-60				
Female	152.2±17.9	$153.4{\pm}18.9$	73.7±19.3*	52.1±1.3*
Male	153.4±19.4	154.6±12.1	74.9±11.9*	52.1±1.1*

Note: * – significant comparative differences (p < 0.05)

At the age of 40-50 years the concentration of T3 hormone in women is 2.30 ± 0.80 , and in men: 2.30 ± 0.12 (nmol/L) (Table 6); the level of T4 hormone in women is 151.30 ± 18.40 , and in men: 153.40 ± 21.60 (nmol/L); the TSH concentration in women is 2.50 ± 0.80 , and in men: 2.30 ± 0.30 (nmol/L) (Table 7).

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Age (years) /	The established norm	1 month	6 months	12 months		
gender	(nmol/L)	(nmol/L)	(nmol/L)	(nmol/L)		
20-30						
Female	2.30±0.06	3.30±0.07*	8.40±0.90*	11.5±0.7*		
Male	2.40±0.30	3.40±0.06*	8.50±0.50*	11.6±0.7*		
30-40						
Female	2.40±0.10	3.40±0.09*	3.50±0.07*	10.8±0.9*		

Table 8:- TSH hormone of the thyroid gland in the post-Covid-19 period.

Male	2.50±0.03	3.50±0.08*	8.60±0.90*	11.2±0.8*
40-50				
Female	2.50±0.80	3.50 ± 0.60	8.60±1.20*	12.1±1.1*
Male	2.50±0.30	3.50±0.50	8.60±0.90*	11.3±1.2*
50-60				
Female	$2.50{\pm}1.40$	3.50 ± 1.60	8.60±1.90*	11.2±1.3*
Male	2.40±1.50	3.40±1.90	8.50±0.80*	11.7±1.1*

Note: * – significant comparative differences (p < 0.05)

At the age of 50-60 years, the value of T3 hormone in women is 1.84 ± 0.80 , and in men: 1.96 ± 1.20 (Tabl. 6); the concentration of T4 hormone in women is 152.20 ± 17.90 , and in men: 153.40 ± 19.40 (Tabl. 7); the TSH level in women is 2.50 ± 1.40 , and in men: 2.40 ± 1.50 (Tabl. 8).

The administration of the remedy "Angel" for 15 days demonstrated a biological effect of stimulating and readjusting the function of the thyroid gland. The concentrations of T3, T4 and TSH hormones returned to the limits of the physiological norms established in all age categories. The level of hormone T3 was elevated: the established norm: 2.20 ± 0.81 ; in the post-Covid-19 period: 1.10 ± 0.17 and after the administration of the remedy "Angel": 2.30 ± 0.42 (nmol/L) (p < 0.05). T4 hormone concentration was increased: the established norm: 108.30 ± 20.10 ; in the post-Covid-19 period - 50.51 ± 1.10 , and after the administration of the remedy: 110.20 ± 11.40 (nmol/L) (p < 0.05) (Tabl. 9). TSH value was changed too: the established norm: 2.40 ± 0.30 , in the post-Covid-19 period: 11.60 ± 0.70 and after administration of the remedy "Angel": 2.40 ± 0.10 (nmol/L) (p < 0.05) (Tabl. 10).



FIG. 8:- Echo-morphology of the thyroid gland after administration of the remedy "Angel"

		.	Thyroid gla	and hormones		
		T3			T4	
Age (years) / gender	The established norm (nmol/L)	Post- Covid-19 (nmol/L)	15 days after the remedy "Angel" administration (nmol/L)	The established norm (nmol/L)	Post- Covid-19 (nmol/L)	15 days after the remedy "Angel" administration (nmol/L)
20-30						
Female	2.20 ± 0.81	1.10 ± 0.17	2.30 ± 0.42	106.5 ± 22.8	50.4±1.3	109.8±24.6
Male	2.14±0.01	1.20±0.11	2.20±0.10	108.3±20.1	50.5±1.1	110.2±11.4
30-40						
Female	2.30±0.79	1.20 ± 0.14	2.30 ± 0.46	147.8 ± 24.6	52.1±1.1	143.9±18.3
Male	2.35±0.9	1.12±0.17	2.30±1.10	148.4 ± 22.8	51.2±1.2	147.5±22.4
40-50						
Female	$2.30{\pm}1.08$	1.20±0.13	2.30±1.09	151.3±18.4	$50.4{\pm}1.1$	150.6±12.7
Male	2.30±1.12	1.20±0.11	2.30±0.42	153.4±21.6	52.1±1.2	152.3±18.4

Table 9:- T	hyroid function in the	post-Covid-19	period after	administration	of the remedy	"Angel"

50-60						
Female	1.84 ± 0.98	1.11±0.14	2.00±0.31	152.2±17.9	52.1±1.2	151.4±13.6
Male	1.96±1.12	1.14±0.13	2.00±0.29	153.4±19.4	52.1±1.1	152.3±14.3
	1.01	11.00	(0.05)			

Note: * – significant comparative differences (p < 0.05)

Table 10:- Adenohypophysis tropic hormone production in the post-Covid-19 period after administration of the remedy "Angel".

Age (years) / gender	Thyroid-stimulating hormone (TSH)					
	The established norm	Post-Covid-19	15 days after the			
	(nmol/L)	(nmol/L)	remedy "Angel"			
			administration			
			(nmol/L)			
20-30						
Female	2.3±0.6	11.5 ± 0.7	2.4±0.8*			
Male	2.4±0.3	11.6±0.7	$2.4{\pm}0.1*$			
30-40						
Female	2.4±1.1	10.8±0.9	2.4±0.9*			
Male	$2.5{\pm}1.3$	11.2 ± 0.8	2.5±0.8*			
40-50						
Female	$2.5{\pm}1.8$	$12.1{\pm}1.1$	2.5±1.1*			
Male	2.5 ± 1.3	11.3 ± 1.2	2.5±1.4*			
50-60						
Female	$2.5{\pm}1.4$	11.2 ± 1.3	$2.5 \pm 1.1*$			
Male	2.4 ± 1.5	$11.7{\pm}1.1$	2.4±1.9*			

Note: * – significant comparative differences (p < 0.05)

Conclusions:-

Physiological indices in subjects, depending on their age and gender, are manifested in the form of characteristic changes in hormone production:

- 1. at the age of 20-30 years the concentration of T3 hormone in women is 2.20 ± 0.05 and in men: 2.14 ± 0.10 (nmol/L); of 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);
- 2. at the age of 30-40 years the level of T3 hormone in women is 2.30 ± 0.19 , and in men: 2.35 ± 0.19 (nmol/L); the concentration of 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).
- 3. at the age of 40-50 years the concentration of T3 hormone in women is 2.30 ± 0.80 , and in men: 2.30 ± 0.12 (nmol/L); the level of T4 hormone in women is 151.30 ± 18.40 , and in men: 153.40 ± 21.60 (nmol/L); the TSH concentration in women is 2.50 ± 0.80 , and in men: 2.30 ± 0.30 (nmol/L).
- 4. at the age of 50-60 years the concentration of T3 hormone in women is 1.84 ± 0.80 , and in men: 1.96 ± 1.20 (nmol/L); the concentration of T4 hormone 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).
- 5. A decrease in the concentration of T3 and T4 in the hormonal profile studied in both women and men to values of 1.13 ± 0.12 and 50.40 ± 1.10 nmol/L, respectively, may reflect the formation of hypothyroidism. This is also confirmed by the increase in TSH on average from 2.30 ± 0.08 to 11.40 ± 0.60 nmol/L over 12 months.
- 6. The research established that the volume of the thyroid gland in the post-Covid-19 period tended to decrease in both women (the established norm is 17.50 ± 0.20 ; at 1 month: 18.90 ± 0.10 ; at 6 months 17.80 ± 0.40 , and at 12 months: 16.80 ± 0.30 nmol/L) and in men (up to 21.30 ± 0.20 nmol/L) in all age categories.
- 7. In the post-COVID-19 period, the production of thyroid hormones after 1 month tends to increase, after 6 months it stabilizes and after 12 months it decreases (T3 level changes from norm established at the age of 30-40 years: 2.30 ± 0.79 up to post-Covid-19 value 1.20 ± 0.14 nmol/L; T4 concentration: from norm established 147.80 ± 24.60 up to post-Covid-19 value 52.10 ± 1.10 nmol/L). TSH concentration changed from established norm 2.50 ± 1.30 up to post-Covid-19 concentration 11.20 ± 0.80 nmol/L which reconfirms the state of hypothyroidism.
- 8. Administration of the remedy "Angel" for 15 days has shown a biological effect of stimulating and readjusting the function of the thyroid gland. The values of T3, T4 and TSH hormones returned to the limits of the

physiological norms established in all age categories (the level of T3 hormone elevated from 1.10 ± 0.17 in the post-Covid-19 period up to 2.30 ± 0.42 nmol/L after the administration of the remedy "Angel"; T4 hormone concentration changed from 50.51 ± 1.10 in the post-Covid-19 period up to 110.20 ± 11.40 nmol/L after the administration of the remedy "Angel"; TSH retuned from 11.60 ± 0.70 in the post-Covid-19 period to 2.40 ± 0.10 nmol/L after administration of the remedy "Angel").

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