

# Study of the Effect of COVID-19 Infection on Thyroid Tissue State

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**Abstract** The article under discussion evaluates the effect of COVID-19 infection on thyroid tissue in patients without and with a history of thyroid disease according to ultrasound (USG) and histology data. The results showed that in 200 individuals with no history of thyroid disease after undergoing COVID-19, the gland enlarged to degree III in 34% and degree IV in 2%. In those with a history of thyroid disease after COVID-19, multiple nodular changes in the thyroid gland were detected, and histological examination confirmed thyroid cancer in 2% of patients.

**Keywords** Coronavirus infection, COVID-19, Thyroid gland, Thyroiditis

## 1. The Relevance of the Research Topic

COVID-19 and its complications continue to be a global problem worldwide [13]. Patients with comorbidities, especially endocrine diseases, have a more severe course of this disease. Thyroid dysfunction is manifested both during the acute phase of COVID -19 infection and during the recovery period after COVID-19, as reported in some literature [8]. Many authors believe, that the thyroid dysfunction induced in COVID - 19 patients is due to the effects of a "cytokine storm" causing autoimmune diseases of the thyroid gland [17], even an exacerbation of Graves' disease has been reported [2]. In patients with thyroid diseases are already known changes in the immune system, weakening of immunity [19]. It has been proven in a number of scientific works that the Fergana Valley is a region with severe iodine deficiency [5]. Iodine deficiency will inevitably have its own features in COVID - 19 disease, especially in patients with pre-existing thyroid diseases. Scientific studies related to iodine-deficient COVID-19 infection have been insufficient worldwide, and the study of thyroid function after COVID-19 infection in people with autoimmune thyroid diseases and nodular and multinodular goitre in Fergana region, which is an iodine deficiency zone, is of great importance. It is necessary to conduct additional informational and scientific studies on this issue in order to deeply understand the influence and mechanisms of pathogenesis of COVID-19 in the acute phase and late stages of the disease on the development and late stage of thyroid diseases, as well as to develop effective recommendations for treatment and clinical control. Taking into account the

above mentioned, the study of the peculiarities of the course of COVID-19 infection in patients with thyroid diseases was recognised as one of the urgent medical issues in our region, especially in Fergana region.

**The aim of the research:** to evaluate the effect of COVID-19 infection on thyroid tissue.

## 2. Objects and Methods of the Research

The data on morbidity among residents of Fergana region of 350 patients who applied to the private clinic of "Doctor Fatkhullo" LLC in 2019-2023 were analysed. Among the patients examined, 295 (84%) were female and 55(14%) were male, whose age ranged from 18 to 73 years.

The patients' disease data were scrutinised to determine the duration of disease course, whether thyroid disease was diagnosed before COVID-19 infection, the patients' general clinical presentation, palpation of the thyroid gland and determination of the degree of enlargement according to WHO classification, determination of thyroid tissue status by ultrasound and evaluation of findings according to TIRADS classification, if thyroid nodules were present to conduct histological fine-needle aspiration biopsy and evaluation of it.

Patients were divided into 2 groups during the period of achievement of these scores. Group 1 consisted of 200 patients with a history of thyroid disease before COVID-19 infection (200 patients, average age  $39 \pm 13.6$  years). Patients in this group were treated for various thyroid diseases under the supervision of an endocrinologist before COVID-19 infection. They had degree I thyroid enlargement (52 patients), degree II enlargement (42 patients), autoimmune thyroiditis (30 patients), nodular goiter (14 patients), mixed goiter disease (10 patients), hypothyroidism (8 patients), subclinical hyperthyroidism (20 patients), there were cases

of diffuse toxic goiter (24 patients).

Group 2 included 150 patients with COVID-19 infection who had no history of thyroid disease. Patients in this group were not under the care of an endocrinologist before COVID-19 infection. A general clinical examination of all patients was performed, including palpation of the thyroid gland, ultrasound of the regional lymph node outflow area and thyroid gland, detection of nodules in thyroid tissue according to TIRADS category, fine-needle aspiration biopsy if nodules were present and histological studies.

### 3. Results Obtained

Thyroid diseases in group 1 patients before COVID-19 infection are presented in table 1 below.

Thyroid level 0 was not observed in any patient of group 1 according to WHO classification, 69 (34,5%) patients had thyroid enlargement of degree I, 131 (65,5%) patients had thyroid enlargement of degree II.

In group 2, 10 (7%) patients with no history of thyroid disease had thyroid degree 0, 95 (63%) patients had thyroid degree I, and 45 (28%) patients had thyroid degree II (Table 3).

As shown in Table 2, patients with a history of thyroid disease were found to have a higher percentage of thyroid enlargement compared to patients in group 2. Degree II thyroid enlargement was found in 131 patients in group 1, that is, patients with pre-existing thyroid disease, and 45

patients in group 2. However, group 1 patients were found to have 2.5 times more degree II thyroid enlargement than group 2 patients. Thyroid enlargement is certainly related to the fact that Fergana region is a region with a high level of iodine deficiency [Ismailov Si ...]. But the fact that COVID-19 affects thyroid tissue is not an exception. Considering the information about the effect of COVID-19 on thyroid tissue in the literature on this subject, we continued our research. At the next stage we studied the thyroid gland condition by ultrasound in patients of both groups, compared and evaluated the changes. When analysing the state of the thyroid gland in group 1 patients who were under the supervision of an endocrinologist before COVID-19 infection, we found diffuse enlargement of the gland of degree I in 52 (26%) patients, enlargement of the thyroid gland of degree II in 42 (21%) patients, autoimmune thyroiditis in 30 (15%) patients, nodular goiter was detected in 14 (7%) patients, mixed goiter in 10 (5%) patients and diffuse toxic goiter in 14 (7%) patients.

In group 2 patients, i.e. patients with no history of thyroid disease, diffuse thyroid enlargement of degree I was observed in 32 (21%) patients, thyroid enlargement of degree II was observed in 45 (30%) patients, autoimmune thyroiditis was observed in 15 (10%) patients, nodular Taurus 8 (5%) patients, mixed Taurus 11 (8%), multinodular goiter was found in 3 (2%) patients and diffuse toxic goiter was found in 6 (4%) patients.

**Table 1.** Diseases detected in the thyroid prior to COVID-19 infection

Group	D1	D2	AIT	Nodular goitre	Mixed goitre	Manifest hypothyroidism	Subclinical hyperthyroidism	DTZ	Total
<b>Group 1 with thyroid disease n=200</b>	52 26%	42 21%	30 15%	14 7%	10 5%	8 4%	20 10%	24 12%	1 100%

**Table 2.** Thyroid diseases after COVID - 19 infection in the examined patients

Groups	Diffuse goitre of degree I	Diffuse goitre of degree II	Autoimmune goitre	Nodular goitre	Mixed goitre	Multinodular goitre	Diffuse toxic goitre	№
<b>Group1 with thyroid disease n=200</b>	22 (11%)	47 (23,5%)	48 (24%)	18 (9%)	20 (10%)	15 (7,5%)	30 (15%)	200
<b>Group 2 without thyroid disease n=150</b>	41 (27%)	45 (30%)	30 (20%)	8 (5%)	11 (8%)	3 (2%)	12 (8%)	150
<b>Total</b>	63	92	78	26	31	18	42	350

**Table 3.** Degree of thyroid gland enlargement according to WHO classification in the examined patients, palpation results

Group №		Level of thyroid gland enlargement			Total
		Degree 0	Degree I	Degree II	
<b>Group 1</b>	Patients who underwent COVID-19 with thyroid disease in anamnesis number 200	0 (0%)	69 (34,5%)	131 (65,5%)	200 (100%)
<b>Group 2</b>	Patients who underwent COVID-19 without a history of thyroid disease number 150	10 (7%)	95 (63%)	45 (28%)	150 (100%)
	Total	10 (3%)	164 (47%)	176 (50%)	350 (100%)

**Table 4.** Frequency of thyroid enlargement after ultrasound in the patients undergoing examination

Group №	Diffuse goitre degree II		Autoimmune thyroiditis	Nodular goitre	Mixed goitre	Multinodular goitre	Diffuse toxic goitre
Group 1	52 (26%)	42 (21%)	30 (15%)	14 (7%)	10 (5%)	10 (5%)	14 (7%)
Group 2	32 (21%)	45 (30%)	15 (10%)	8 (5%)	11 (8%)	3 (2%)	6 (4%)

**Table 5.** Distribution of nodular derivations in the thyroid gland according to TIRADS category using ultrasound in the examined patients

Groups	TIRADS-I	TIRADS-II	TIRADS-III	TIRADS-IV	TIRADS-V	Total
Group 1 with thyroid disease n=46	0 (0%)	24 (52%)	12 (26%)	8 (17%)	2 (4%)	46 (100%)
Group 2 without thyroid disease n=22	0 (0%)	16 (72%)	5 (23%)	1 (5%)	0 (0%)	22 (100%)
Total		39 (57%)	17 (25%)	10 (15%)	2 (3%)	68 (100%)

**Table 6.** Comparative evaluation of thyroid tissue examination using ultrasound in thyroid parenchyma after COVID-19 infection involving both groups

Groups	Nodular goiter	Mixed goiter	Multinodular goiter	Histology Thyroid cancer	Total
Group 1 with thyroid disease n=200	18 (9%)	20 (10%)	8 (4%) Total (23%)	2	46
Group 2 without thyroid disease n=150	8 (5%)	11 (8%)	3 (2%) Total (15%)		22
Total	26	31	11	2	68

From the results, it can be seen that degree I thyroid enlargement in patients with history of thyroid disease in group 1 who had COVID-19 infection was observed in 22 (11%) patients, degree II thyroid enlargement in 47 (23, 5%) patients, AIT in 48 (24%) patients, nodular goiter in 18 (9%) patients, mixed goiter in 20 (10%) patients, multinodular goiter in 15 (7.5%) patients, and diffuse toxic goiter in 30 (15%) patients. Interestingly, in patients with thyroid changes after COVID-19 infection it was found that diffuse goiter decreased and mixed, nodular and multinodular forms of goiter increased. The effect of COVID-19 infection on thyroid tissue structure is also mentioned in the world literature.

In group 2 patients, i.e. patients with no history of thyroid disease, diffuse thyroid enlargement of degree I was observed in 41 (27%) patients, thyroid enlargement of degree II was observed in 45 (30%) patients, autoimmune thyroiditis was observed in 30 (20%) patients, nodular goiter in 8 (5%) patients, mixed goiter in 11 (8%) patients, multinodular goiter was diagnosed in 3 (2%) patients, and diffuse toxic goiter was diagnosed in 12 (8%) patients. While patients in this group did not have any thyroid parenchyma disease prior to COVID-19 infection, the results obtained in the above group of patients with thyroid disease support our assumption. The results obtained in both groups indicate that most of the changes in thyroid structure were nodular, multinodular and mixed in type. Interestingly, the question was whether this condition was a complication of iodine deficiency or a complication of COVID-19. When we analysed by TIRADS, it was found that the nodules had the following categories. No nodule corresponded to TIRADS-I category in patients with a history of thyroid disease in group 1 who had COVID-19 infection. The TIRADS-II category accounted for 24 (52%) nodules. Twelve (26%) nodules

were found to correspond to TIRADS-III category. Thyroid nodule of 8 (17%) patients corresponded to TIRADS-IV category. However, TIRADS-V category corresponded to thyroid nodule in 2 (4%) patients.

No nodule corresponded to the TIRADS-I category even in group 2 patients, that is, patients with no history of thyroid disease. TIRADS-II category accounted for 16 (72%) nodules. It was found that 5 (23%) nodules corresponded to TIRADS-III category. Thyroid nodule in 1 (5%) patient corresponded to TIRADS-IV category. On the other hand, TIRADS-V category was not found in any patient. From this, it can be seen that patients with a history of thyroid disease in group 1 who had COVID-19 infection showed higher TIRADS categories compared to patients in group 2, implying that nodularity of patients in this group indicates higher malignancy. The results of this validation are presented in Table 5.

The patients in our study were categorised as follows: thyroid diseases detected by ultrasound at a later stage.

Based on the ultrasound screening method, 46 of 200 patients in group 1 who had a history of Covid-19 infection with thyroid disease and 22 of patients in group 2 who had no history of thyroid disease were referred for fine-needle aspiration biopsy. They revealed 3,4,5 levels of TIRADS category. According to the biopsy results, thyroid nodular masses in 2 patients with a history of thyroid disease in group 1 corresponded to TIRADS-V category. Histological examination confirmed the presence of thyroid cancer.

These results showed increased nodular changes in thyroid tissue after COVID-19 infection in patients with and without a history of thyroid disease, while patients with pre-existing thyroid disease developed cancer in 2 patients on histological examination. This suggests an adverse effect of COVID-19

infection on thyroid tissue. We believe that the role of iodine deficiency plays a special role in these changes and further studies are needed to provide evidence in this regard.

## 4. Conclusions

1. It was found that individuals with no history of thyroid disease who underwent COVID-19 in Fergana region developed autoimmune thyroiditis in 10%, nodular goiter in 5%, mixed goiter in 8%, multinodular goiter in 2% and diffuse toxic goiter in 4% after COVID-19. Thyroid AIT in patients with a history of pre-existing thyroid disease was found in 19%, nodular goiter in 9%, mixed goiter in 10%, multinodular goiter in 4% and diffuse goiter in 16% of patients.
2. In those with no history of thyroid disease who underwent COVID-19 infection, nodular masses in thyroid tissue corresponded to 23% of patients in TIRADS-III category and 5% of patients in TIRADS-IV category after COVID-19. In patients with a history of thyroid disease, nodular masses in thyroid tissue corresponded to the TIRADS-III category in 26%, TIRADS-IV category in 17% and TIRADS-V category in 4% of patients. This shows that patients in this group have higher risk of malignancy.
3. COVID-19 infection tends to develop autoimmune and nodular neoplasms in the thyroid gland. However, people with pre-existing thyroid disease were found to have an increased risk of developing cancer in nodular neoplasms, and 2 patients were confirmed to have thyroid cancer.
4. Patients with COVID-19 have a high risk of autoimmune and nodular malignancies in thyroid tissue during early and prolonged periods of recovery, indicating the importance of monitoring thyroid function.

The fact that our studies were conducted in an area of iodine deficiency, and the literature indicates that iodine deficiency is a risk factor for thyroid cancer, suggests that COVID-19 infection causes not only autoimmunity but also accelerated cancerous processes in thyroid tissue. We believe that it is important to monitor thyroid function and tissue status during the early and long-term recovery period in people with COVID-19. Given the high risk of nodule formation and malignancy, especially in patients with a history of thyroid disease, it is important to perform COVID-19 and include it in the follow-up protocol based on the results obtained.

The literature indicates that the cytokine storm that occurs during the acute period of COVID-19 infection activates autoimmune factors, causing autoimmune processes in the thyroid cell, in particular the development of autoimmune thyroiditis, Graves' disease [7]. However, in COVID-19 survivors, the activation of autoimmune processes in thyroid tissue, in particular the development of nodular goiter and even heel cancer, indicates that the infection may be caused

by cell growth factors [11].

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