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INVESTIGATING THYROID HORMONE IMBALANCES IN COVID-19 PATIENTS FROM LARKANA

Ishfaque Ahmed Mugheri[1], Abdul Majid[*1], Qamar Abbas Solangi[2], Dr Javed Ali Khawaja[3], Vinay Kumar Jesrani[4], Mehar Ali Kazi[5]

[1]*Department of Biochemistry, Shah Abdul Latif University, Khairpur.*
[2]*Department of Biology, College of Science, University of Bahrain, Kingdom of Bahrain.*
[3]*Jacobabad Institute of Medical Sciences (JIMS).*
[4]*Department of Biochemistry, Chandka Medical College SMBBMU Larkana.*
[5]*Institute of Biochemistry, University of Sindh, Jamshoro*

[1]amajid.ansari@salu.edu.pk

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Corresponding Author: *
Abdul Majid

Abstract

Objective: *The objective of the study was to assess thyroid function tests in patients hospitalized with COVID-19 and examine how these results influenced the progression of the disease.*

Study Design: *This cross-sectional study was conducted between 2022 and 2023 in Larkana, Sindh, Pakistan. It involved 129 COVID-19-positive patients who were hospitalized in the COVID-19 ward and treated at private clinics.*

Methodology: *T3, T4, and TSH thyroid function tests, together with other initial investigations, were performed on Covid-19 patients. Patients with prior thyroid-related conditions were disqualified, as were those with unreported prior outcomes. Vaccination status was confirmed by collecting the vaccine card. The data was analysed using SPSS version 26.*

Results: *A study of 129 individuals found that 51% experienced tiredness, depression, constipation, and muscle soreness. Gender differences were observed in weight distribution, with males having a higher proportion of normal weight and overweight individuals. Thyroid-related indicators showed varied distributions, highlighting significant changes in thyroid function.*

Conclusion: *This study concluded that the thyroid function can be disrupted in all patient groups during a COVID-19 infection, even in individuals without pre-existing thyroid issues. This preliminary study suggests that changes in blood levels of T3, T4, and TSH could serve as important indicators of COVID-19 pneumonia*

INTRODUCTION

COVID-19 is a viral illness triggered by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). The outbreak of this fatal disease affected more than 36 million individuals globally in 2019, leading the World Health Organization (WHO) to classify it as a public health emergency and subsequently a pandemic. (1) The virus impacts various organs, disrupting their normal functions. (2,3) The main receptor for SARS-CoV-2, angiotensin-converting enzyme 2 (ACE2), is found in numerous endocrine glands. (4) COVID-19 can directly or indirectly cause thyroiditis, with immune

system dysfunction playing a role. (5,6) The infection triggers an immune response, resulting in a cytokine storm through the release of pro inflammatory cytokines. (7) However, thyroid function tests may be altered due to non-thyroidal illnesses during sepsis, with free T3 (FT3) levels decreasing due to the presence of inflammatory cytokines.

The literature offers limited insights into the impact of COVID-19 on the thyroid and adrenal glands. (8) The hypothalamic-pituitary-adrenal axis response varies with systemic illness and can influence treatment, especially when corticosteroids are necessary. Critical Illness-Related Corticosteroid Insufficiency (CIRCI) is characterized by a diminished adrenal response, dependent on the severity of illness and inflammation (7), although some patients may exhibit an increased cortisol response. Tan et al. observed elevated plasma cortisol levels in COVID-19 patients and noted a higher mortality rate compared to those without the virus. A postmortem study highlighted severe adrenal damage in patients who had succumbed to COVID-19, emphasizing the importance of monitoring adrenal function both during acute infection and post-recovery. (8) When Dr. Ji-Xian Zhang of the Hubei Clinic of Coordinated Conventional Chinese and Western Medicine diagnosed pneumonia in an elderly couple on December 26, 2019, it was originally unclear what was causing their illness. Five additional people with comparable symptoms were discovered the next day; the majority of them had ties to the Huanan Seafood Market. The Hubei Provincial Health Committee was notified of the problem on December 29. According to a review of these early cases conducted in the past, SARS-CoV-2 has been extensively spreading in Wuhan since mid-December 2019 (7).The COVID-19 pandemic, initially a regional outbreak, escalated into a global emergency, with 144 nations, territories, and regions reporting cases as of March 15, 2020, with predictions subject to variation (7).

Methodology

A cross-sectional study was carried out to assess different health parameters in COVID-19 patients from Shaheed Mohtarama Benazir Bhutto Medical University (SMBBUM) Larkana and private clinics in the Larkana area. The study included 129 participants, aged 18 to 60 years, who had been diagnosed with COVID-19. All participants received treatment at either SMBBUM or private hospitals in Larkana. Before participation, each individual was given a comprehensive written consent form, which they signed to confirm their voluntary involvement. The primary aim of the study was to collect data on various health outcomes related to COVID-19 and associated factors within this particular age group.

Exclusion and inclusion

Individuals with COVID-19 who are between those in the age range of 18 and 60 years, compatible with both sexes, and restricted to the Larkana area No thyroid issues in the past, readiness to participate in the research, this study only included those who tested positive for PCR, and those who tested positive for an ICT fast test were excluded, as were all patients under the age of 18 and those over 60. Patients having an unknown history of prior thyroid levels were not included in this study because they were unwilling to participate.

Sampling

Blood samples were collected using the venipuncture technique with the assistance of a vacationer and tourniquet. Participants were carefully instructed on how to handle the collection equipment without directly touching it, ensuring proper hygiene. To prevent hemolysis and contamination, strict safety protocols were followed throughout the process. A total of 5 ml of blood was drawn and placed into either a plain or gel tube, which was left to clot. The sample was then centrifuged at 4000 RPM for 20 minutes. Following this, the serum (supernatant) was carefully separated and stored at -4°C until it was ready to be tested for the thyroid profile.

Statistical examinations

The data were processed using SPSS version 28. The mean and standard deviation (SD) for both the COVID-19 patients and control groups were computed. A t-test was conducted to compare thyroid function outcomes (normal, high, and low) between male and female COVID-19 patients and controls. A p-value of 0.05 or less was deemed statistically significant for all comparisons.

RESULTS

Table 1.0 show the sample of 129 individuals with a higher proportion of married, educated individuals, with a significant representation across different occupations, particularly in government employment and labor. The majority were married, with 60% being educated and 40% uneducated. The majority completed matric, intermediate, or post-graduate education.

Table 1. Covid-19 Patients' Socio-Demographics Status

Characteristics	Variable	Frequency (n=129)	(%)
Gender	Male	67	52%
	Female	62	48%
Marital Status	Married	96	74%
	Unmarried	33	26%
Literacy	Educated	77	60%
	Uneducated	52	40%
Education Level	Matric	34	44%
	Intermediate	27	35%
	Graduate	9	12%
	Post Graduate	7	9%
Occupation	Govt Employ	43	33%
	Labour	41	32%
	Student	26	20%
	House wife	19	15%

According to table 2.0, 51% (66) of participants reported feeling tired, making it the most often reported symptom. Additionally, depression was very common, affecting 29% (38) of people. Of the sample, 26% (34) reported constipation, and 33% (42) reported muscle soreness. The least prevalent symptom, reported by just 9% of participants, was dry skin, while 20% (26) of individuals felt neck pain (12). These findings show that melancholy and exhaustion were the group's most prevalent symptoms, however a sizable percentage of individuals also had additional symptoms like diarrhea and muscle soreness.

Table 2 Prevalence of Symptoms

Sign And Symptoms	Frequency (n=129)	Percentages (%)
Depression	38	29
Fatigue	66	51
Dry Skin	12	9
Constipation	34	26
Muscle pain	42	33
Neck pain	26	20

The data shows in figure 1.0 that the gender differences in weight distribution, with males having a higher proportion of normal weight and overweight individuals, while females have a higher prevalence of obesity and a slightly greater percentage of underweight individuals. Underweight individuals are more common in males, while females have a higher prevalence of obesity.

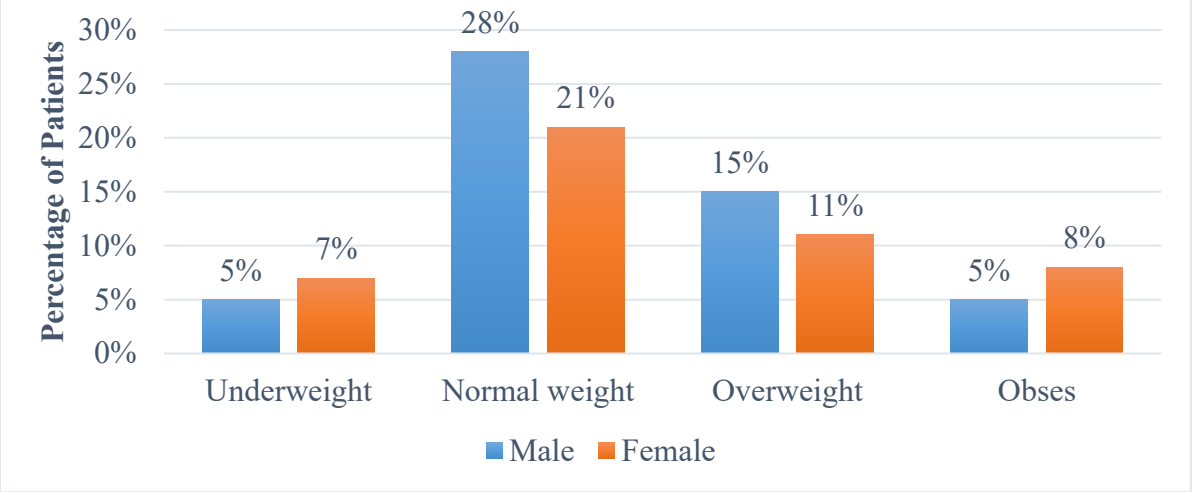

Figure 1 Gender-wise Body Mass Index of COVID-19 patients

The distribution of the data as shows in figure 2.0 the varied percentages of the three thyroid-related indicators (TSH, T3, and T4) at different levels (Normal, High, and Low). For T3, 5% of people have high levels, 12% have low levels, and 73% of people fall within the usual range. At 81%, T4 displays a greater proportion of normal levels, with 10% of people having high levels and 9% having low levels. In contrast, 28% of people have high levels of TSH, 12% have low levels, and 60% of people have levels within the usual range. While TSH shows a significant percentage of people with high levels, this distribution shows a general trend for T3 and T4 markers to be primarily within the normal range.

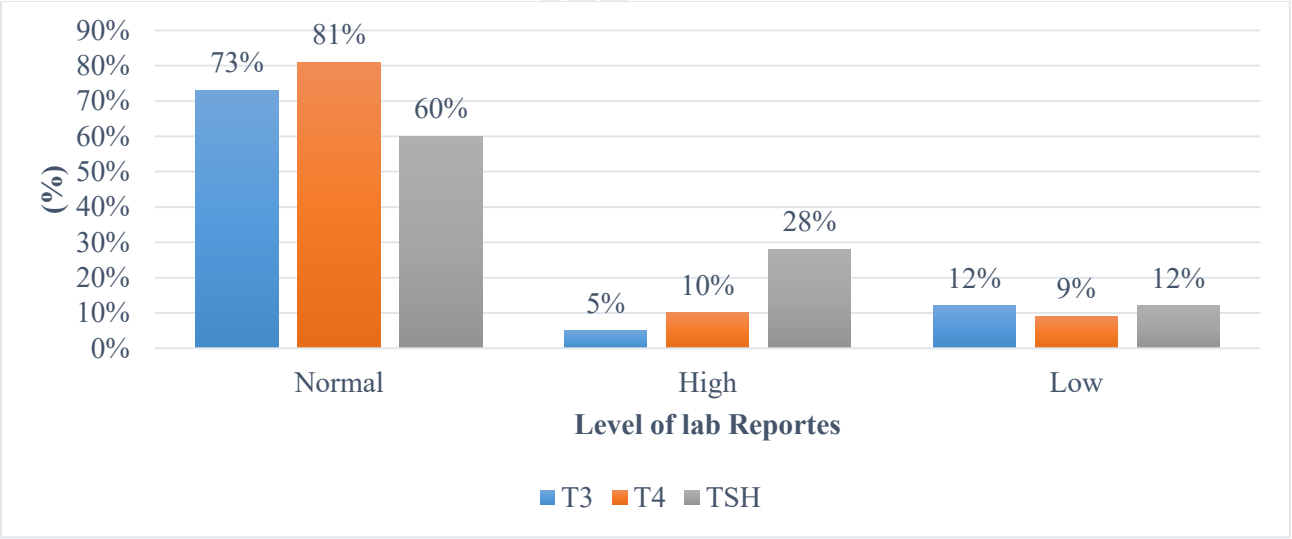

Figure 3.0 Distribution of thyroid Hormone test from Covid-19 patients.

The data show in table 3.0 which compares thyroid function parameters (T3, T4, and TSH) during and after Covid-19. T3 levels decreased significantly during the pandemic, while T4 levels slightly increased. TSH levels also decreased significantly, with T3 levels decreasing and TSH levels lowering after the pandemic. T4 remained stable. Overall, these findings highlight significant changes in thyroid function.

Table 3.0 Comparison of Thyroid Parameters during and After Covid-19

Parameter	During Covid-19 Mean±SD	After Covid-19 Mean±SD	p-value
T3 (0.8-2.0 ng/ml)	1.71±1.02	1.21±0.91	0.04
T4 (5.1-14.1 µg/dl)	8.74±6.64	8.93±6.94	0.07
TSH (0.35-4.94 µIU/ml)	9.15±3.38	4.32±1.72	0.00

DISCUSSION

TSH levels were greater in patients with moderate and severe Covid-19, according to the study's findings when compared to previous data on patient thyroid hormone levels. Furthermore, the rise in T4 levels throughout follow-up appeared to be influenced by the elevated T3 levels seen in these patients. However, a retrospective study carried out in China found that patients with severe Covid-19 had decreased TSH levels. Additionally, the elevated T3 levels observed in these patients seemed to play a role in the increase of their T4 levels during follow-up. In contrast, a retrospective study conducted in China reported lower TSH levels in severely affected Covid-19 patients, while an Italian study identified thyrotoxicosis in Covid-19 patients after their diagnosis was confirmed. These discrepancies highlight the variability in thyroid function changes among Covid-19 patients, suggesting that responses may differ by region (10, 11). Both the Chinese and Italian studies found that thyroid hormone levels generally returned to baseline during follow-up; however, our study observed persistent elevated T3 levels across all severity levels of Covid-19, which contrasts with these findings. This difference raises concerns, especially given the potential long-term damage Covid-19 may inflict on the cardiovascular and respiratory systems (12). Post-infectious sequelae, particularly cardiac issues, may worsen due to thyroid dysfunction. As the thyroid plays a crucial role in regulating various long-term body functions, iodine deficiency-related thyroid problems are a significant concern, particularly in low-income countries. Such imbalances can negatively affect critical systems like the cardiovascular, respiratory, and catabolic functions. The introduction of salt iodization has played a vital role in mitigating these health risks, ensuring adequate iodine intake for maintaining thyroid health (13-14). Covid-19, a newly emerged disease, has led to substantial loss of life in lower-middle-income countries, with the death toll surpassing one million and showing no signs of decreasing (15). As the pandemic continues to unfold, more information is being gathered about the virus's impact on various bodily systems, especially the endocrine system, which could have significant long-term effects. This is particularly concerning for nations already grappling with chronic endocrine diseases (16).

Pakistan appears to have largely avoided the worst impacts of the Covid-19 pandemic, unlike other countries that faced severe effects (17). The thyroid problems found in our study, however, indicate that it is important to consider the long-term implications of COVID-19, particularly in patients who are in critical condition. This is particularly crucial for older patients, whose symptoms—like raised TT3 levels, body pains, disorientation, and an elevated heart rate—may be wrongly ascribed to viral infection recovery. The thyroid storm, which is typified by elevated inflammatory markers, can occasionally coexist with the cytokine storm that frequently accompanies COVID-19 in critically sick patients (18). Similar thyroid abnormalities produced by another coronavirus were found in post-mortem thyroid tissue tests from SARS patients during the 2002 pandemic. (19). Additionally, the use of corticosteroids to treat severe Covid-19 could potentially lead to autoimmune damage to the thyroid gland, complicating recovery due to the overlap of immunogenic and hormonal factors in this rare disease (19).

Patients with Covid-19 have been observed to exhibit reduced TSH levels, with two main theories proposed to explain this phenomenon (20). One theory suggests direct damage to the thyroid follicles by SARS-CoV-2, while another points to pituitary dysfunction as the more likely cause of thyroid tissue destruction (21). In critically ill individuals, thyroid dysfunction, known as sick euthyroid syndrome, is commonly observed. Differences in peripheral thyroid hormone uptake, thyroid hormone binding to transport proteins, and

TSH secretion are all involved in this disorder. Treating sick euthyroid syndrome with thyroid hormones is typically futile since it is a pathological reaction to acute sickness (22). The impact of COVID-19 on ill euthyroid syndrome has been the subject of numerous studies (23, 24). TSH levels were significantly higher and T3 levels were significantly lower in individuals with Covid-19 pneumonia than in those with non-Covid-19 pneumonia of comparable severity. Covid-19 differs from sick euthyroidism, in our opinion, because it impacts thyroid function and acute phase reactants irrespective of the severity of the illness. This study, the first of its type in Sindh's Larkana, looked at the thyroid hormone levels of individuals with COVID-19 though it had some limitations, including a short follow-up period and the lack of baseline tests for free T3, free T4, or other pituitary hormones at the time of admission. Our tertiary care hospital primarily treated severe Covid-19 cases, and thyroid function was not assessed in patients with mild Covid-19.

CONCLUSION

In conclusion, this study sheds important light on the wider consequences of COVID-19 by highlighting the higher risk of thyroid hormone abnormalities in patients. It emphasizes how crucial clinical care is for tracking thyroid function during recovering. Both those who received the vaccination and those who did not showed changes in thyroid hormone levels. This emphasizes the significance of continuous attention to thyroid health management both during and after COVID-19 recovery.

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