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Original Article

The impact of COVID-19 infection on thyroid function

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Abstract

Extensive research on COVID-19 has revealed a notable link between the disease and thyroid disorders, highlighting complex interactions between thyroid hormones, immunomodulatory signaling molecules within the thyroid gland, and viral infections. This study evaluated the relationship between thyroid function and COVID-19 in Iraqi patients at Adiwaniyah Teaching Hospital. The cohort for this investigation comprised all patients who were admitted to the isolation center at the Teaching Hospital during the timeframe extending from January 2024 to June 2024. Each participant included in this research underwent comprehensive evaluations of their thyroid function, which is composed of the measurement of thyroid-stimulating hormone (TSH), total triiodothyronine (T3), and serum total thyroxine (T4) levels. Results showed that the serum T4 levels in all participants included in the study were observed to range from 20 to 182 (ng/dl), with the average concentration recorded at 87.26 ± 38.29 (ng/dl); no statistically significant disparity was noted in the mean serum T4 levels relative to the severity of the disease ($p = 0.291$). The serum TSH levels across all enrolled individuals spanned from 0.03 to 82 (mU/L), with a mean concentration of 5.55 ± 12.36 (mU/L); similarly, there was no statistically significant difference in the mean serum TSH levels when assessed against the disease severity ($p = 0.926$). According to the serum thyroid hormone concentrations, the cohort was stratified into 17 (24.6%) individuals classified as hypothyroid, 34 (49.3%) categorized as euthyroid, and 18 (26.1%) identified as hyperthyroid. Furthermore, no significant correlation was identified between the disease's severity and the participants' thyroid status ($p = 0.556$). In conclusion, patients with COVID-19 are liable to develop thyroid function abnormalities that may explain several of the long-term symptoms associated with the disease.

Keywords: COVID-19, Euthyroid, Thyroid dysfunction, Thyroxine, Triiodothyronine

1. Introduction

The Coronavirus Disease 2019 (COVID-19) represents a pandemic of the new millennium that represents exceptional challenges to public health [1, 2]. The etiological agent is an emergent enveloped β-coronavirus identified as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [3, 4]. Following its initial identification in Wuhan, COVID-19 has disseminated rapidly, leading to a substantial increase in outbreak occurrences. The infection caused by SARS-CoV-2, which manifests as COVID-19, has impacted over 670 million individuals globally as of January 2023 [5]. By April 2022, COVID-19 was linked to over 6.2 million fatalities worldwide, a figure which is presumed to be underestimated [6]. SARS-CoV-2 exhibits a phylogenetic affinity with SARS-CoV-1 and maintains a relationship with SARS-CoV-1 [7]. The mechanism of SARS-CoV-2 infection in human tissues involves entry into cells via the angiotensin-converting enzyme 2 (ACE2) receptor [8].

COVID-19 presents a spectrum of clinical manifestations, ranging from asymptomatic cases to severe and potentially lethal respiratory complications [9]. A considerable volume of research has been conducted across various dimensions of the disease, encompassing prevention, diagnosis, and therapeutic interventions; these extensive investigations into COVID-19 have culminated in an expanding corpus of evidence that highlights a significant correlation between the incidence of thyroid disorders among individuals afflicted with COVID-19 [10-13].

A multifaceted relationship has been elucidated between hormonal interactions and immunomodulatory signaling entities in the context of thyroid pathologies and viral infections [14]. The influence of viruses and their consequent inflammatory-immune responses is particularly significant, as it has been observed to induce permanent alterations in thyroid function in specific instances [15]. Despite numerous investigations assessing thyroid gland functionality amidst the COVID-19 pandemic on a global scale, there exists a lack of knowledge regarding such a relationship in the Iraqi population; consequently, we undertook the present study to examine the correlation between thyroid function and COVID-19 among a cohort of Iraqi patients.

2. Material and Methods

This observational cross-sectional study was conducted at a single center at the Adiwaniyah Teaching Hospital in Adiwaniyah Province, Iraq. The study encompassed

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all patients who were admitted to the isolation center of the Teaching Hospital during the timeframe from January 2024 to June 2024. The criteria for inclusion consisted of patients exhibiting positive findings on high-resolution computed tomography (HRCT), such as consolidation, linear opacity, septal thickening, crazy-paving pattern, or halo sign, as well as patients with confirmed COVID-19 via polymerase chain reaction (PCR). The criteria for exclusion were delineated as follows: individuals with a prior diagnosis of thyroid disease, pregnant women, and those patients who declined participation in the study.

Informed consent was duly secured from all individuals involved in the study, and the research protocol received endorsement from the institutional review board of the College of Medicine in the Province. A cumulative total of 69 patients were recruited for participation in this investigation.

All subjects participating in the investigation underwent comprehensive evaluations of their thyroid function parameters, including thyroid-stimulating hormone (TSH), total triiodothyronine (T3), and serum total thyroxine (T4) concentrations, which were assessed utilizing electro-chemical-luminescent immunoassay (ECLIA) within the Elecsys® 2010 immunoassay platform. Any departure from the established normal reference range indicated thyroid dysfunction.

All cases were categorized as moderate, severe, or critical according to clinical manifestations, laboratory evaluations, and chest computed tomography (CT) imaging. Moderate and severe cases were defined as exhibiting pneumonia-related signs observable on imaging, a respiratory rate of ≥ 30 breaths per minute, and an oxygen saturation level of ≤ 90% while at rest. Critical cases were designated as those necessitating mechanical ventilation owing to respiratory failure, the presence of other organ dysfunctions requiring intensive care unit management, and the occurrence of shock.

The data were analyzed utilizing the Statistical Package for the Social Sciences (SPSS) version 26 (IBM Corp., Armonk, NY, USA). Quantitative variables were articulated as mean ± standard deviation (SD), while qualitative variables were expressed in terms of frequency and percentages. The two groups' comparative analysis was performed using the student's t-test and Chi-square test when appropriate. A receiver operating characteristic (ROC) curve was generated for assessing thyroid function tests and acute phase reactants to determine the sensitivity and specificity of the laboratory parameters in the context of COVID-19 pneumonia. A P-value threshold of less than 0.05 was deemed statistically significant.

3. Results

The demographic attributes of patients diagnosed with COVID-19 who participated in the study are presented in Table 1. The ages of all participants ranged from 22 to 70 years, with a mean age of 46.01 ± 14.89 years. Based on disease severity, the patients were categorized into three distinct groups: moderate (n = 35), severe (n = 19), and critical (n = 15). Examining mean age incidence with disease severity shows no statistically significant differences (p = 0.872). The study comprised 21 (30.4%) males and 48 (69.6%) females, and the analysis of sex distribution by disease severity demonstrated no significant disparities (p = 0.672).

The serum levels of thyroid hormones (T3 and T4) and thyroid stimulating hormone (TSH) are demonstrated in Table 2. The T3 in all enrolled patients was in the range of 0.4 -8.4 (nmol/L) and the mean level was 1.57 ±1.19 (nmol/L); there was no significant difference in mean serum T3 based on the severity of the disease (p = 0.438).

The T4 in all enrolled patients was in the range of 20 -182 (ng/dl) and the mean level was 87.26 ±38.29 (ng/

Table 1. The demographic characteristic of COVID-19 patients enrolled in the study.

Characteristic	Total (*n* = 69)	Moderate (*n* = 35)	Severe (*n* = 19)	Critical (*n* = 15)	*p*
Age (years)					
Mean ± SD	46.01 ± 14.89	46.57 ± 15.07	44.47 ± 16.36	46.67 ± 13.29	0.872 O
Range	22 - 70	22 - 70	22 - 69	24 - 67	NS
Sex					
Male, *n* (%)	21 (30.4 %)	9 (25.7 %)	7 (36.8 %)	5 (33.3 %)	0.672 O
Female, *n* (%)	48 (69.6 %)	26 (74.3 %)	12 (63.2 %)	10 (66.7 %)	NS

n: number of cases; SD: standard deviation; O: one-way ANOVA; C: chi-square test; NS: not significant.

Table 2. Comparison of mean serum T3, T4 and TSH based on the severity of COVID-19.

Characteristic	Total (*n* = 69)	Moderate (*n* = 35)	Severe (*n* = 19)	Critical (*n* = 15)	*p*
T3 (nmol/L)					
Mean ± SD	1.57 ± 1.19	1.43 ± 0.81	1.55 ± 1.04	1.91 ± 1.92	0.438 O
Range	0.4 - 8.4	0.4 - 3.6	0.5 - 4.2	0.4 - 8.4	NS
T4 (ng/dl)					
Mean ± SD	87.26 ± 38.29	80.89 ±36.02	89.57 ± 40.15	99.19 ± 40.44	0.291 O
Range	20 - 182	20 - 147	40 - 145	28.8 - 182	NS
TSH (mU/L)					
Mean ± SD	5.55 ± 12.36	6.09 ±14.99	5.28 ± 7.99	4.63 ± 10.63	0.926 O
Range	0.03 - 82	0.03 - 82	0.04 - 28.6	0.03 - 41.4	NS

n: number of cases; SD: standard deviation; O: one-way ANOVA; C: chi-square test; NS: not significant.

dl); there was no significant difference in mean serum T4 based on the severity of the disease ($p = 0.291$). The TSH in all enrolled patients was in the range of 0.03 -82 (mU/L) and the mean level was 5.55 ±12.36 (mU/L); there was no significant difference in mean serum TSH based on the severity of the disease ($p = 0.926$).

Based on the serum levels of thyroid hormones, patients were categorized into 17 (24.6 %) hypothyroid patients, 34 (49.3 %) euthyroid patients, and 18 (26.1 %) hyperthyroid patients. There was no significant association between the severity of the disease and thyroid status ($p = 0.556$), as shown in Table 3.

A comparison of mean age and sex proportions based on thyroid status is shown in Table 4. There was a significant difference in mean age according to thyroid status ($p = 0.030$); the highest mean age was reported in patients with euthyroid status and patients with hypothyroid and hyperthyroid status had a mean age that was significantly lower than that of patients with euthyroid status, 42.24 ±13.62 years and 40.67 ±14.23 years versus 50.74 ±14.71 years, respectively.

4. Discussion

The thyroid gland constitutes a pivotal organ in sustaining numerous long-term physiological functions of the organism, particularly concerning cardiovascular, respiratory, and catabolic processes; consequently, numerous lower-income nations have instituted salt iodination as a strategy to mitigate the ramifications of iodine-deficient thyroid pathologies [16, 17]. As a novel infectious disease, COVID-19 has inflicted a catastrophic impact on lower-middle-income nations, with a seemingly unending trajectory regarding the escalating mortality rate, which, at the time of this composition, is projected to surpass 1,000,000 [18]. As the pandemic continues unabated, an increasing array of insights is being uncovered, not only regarding the multi-systemic engagement of the virus but also concerning its disruption of the endocrine system. Such long-term repercussions can no longer be disregarded, particularly in the framework of nations that are already grappling with widespread endocrine disorders [19].

Given the thyroid dysfunctions that have been identified within our study cohort, it appears that the long-term ramifications of COVID-19, particularly concerning the longitudinal assessment of COVID-19 survivors, may be inadequately addressed, especially among the elderly demographic, for whom manifestations of elevated T3 levels in the bloodstream—such as myalgia, cognitive disorientation, and tachycardia—could be erroneously interpreted as mere recovery from a viral illness. Simultaneously, a thyroid storm characterized by elevated inflammatory markers exhibits overlapping clinical presentations with the cytokine storm typically associated with the exacerbation of COVID-19 in critically ill individuals [20-22]. Indeed, there exists a precedent for the impact of prior coronaviruses on thyroid function, as evidenced by post-mortem analyses of thyroid tissues from individuals afflicted with SARS during the 2002 outbreak. This immunological and endocrine interplay associated with a novel pathogen may further complicate the therapeutic management and recovery of COVID-19, as the corticosteroids administered to treat severe COVID-19 may inadvertently induce autoimmune damage to the thyroid gland [23].

In our investigation, we observed that a noteworthy segment of individuals afflicted with COVID-19 exhibited alterations in serum thyroid hormone concentrations as well as serum TSH levels, indicative of primary hypothyroid status. Consistent with our findings, Malik et al. [24] reported that TSH levels were elevated in patients experiencing moderate to severe manifestations of COVID-19 when contrasted with those not infected by the virus. Furthermore, we ascertained that a considerable proportion of our patient cohort presented with indications of hyperthyroid status, which appeared to be primary in nature, based on the analysis of serum thyroid hormones and serum TSH levels. Malik et al. [24] also noted that T3 levels were significantly elevated during follow-up assessments in COVID-19 patients relative to non-COVID-19 individuals, with minimal to non-observable impact on T4 levels. Consequently, we concur with Malik et al. [24] that COVID-19 infection may influence the thyroid gland through various mechanisms, resulting in either hypothyroid or hyperthyroid.

Additionally, a comparable retrospective investigation conducted in China revealed diminished TSH levels in patients suffering from severe cases of COVID-19,

Table 3. The relationship between thyroid status and severity of COVID-19.

Characteristic Thyroid status	Total ($n = 69$)	Moderate ($n = 35$)	Severe ($n = 19$)	Critical ($n = 15$)	p
Hypothyroidism	17 (24.6 %)	9 (25.7 %)	6 (31.6 %)	2 (13.3 %)	0.556 C NS
Euthyroid status	34 (49.3 %)	19 (54.3 %)	7 (36.8 %)	8 (53.3 %)	
Hyperthyroidism	18 (26.1 %)	7 (20.0 %)	6 (31.6 %)	5 (33.3 %)	

n: number of cases; C: chi-square test; NS: not significant.

Table 4. Comparison of mean age and sex proportions based on thyroid status.

Characteristic	Euthyroid status ($n = 34$)	Hypothyroidism ($n = 17$)	Hyperthyroidism ($n = 18$)	p
Age (years)				
Mean ± SD	50.74 ± 14.71	42.24 ± 13.62	40.67 ± 14.23	0.030 O
Range	22 - 70	22 - 70	22 - 68	*
Sex				
Male, *n* (%)	10 (29.4 %)	4 (23.5 %)	7 (38.9 %)	0.604 O
Female, *n* (%)	24 (70.6 %)	13 (76.5 %)	11 (61.1 %)	NS

n: number of cases; SD: standard deviation; O: one-way ANOVA; C: chi-square test; NS: not significant; *: significant.

alongside a study from Italy that identified instances of thyrotoxicosis in COVID-19 patients' post-confirmation of their diagnosis [25, 26]. In the aforementioned Chinese study, encompassing 50 patients diagnosed with moderate to critical COVID-19 without prior thyroid disease history, Chen et al. reported that over 60% exhibited altered thyroid function. The most prevalent abnormalities detected among these patients were low TSH levels, occurring with or without concomitant reductions in total T3 (tT3) levels [2].

A research investigation indicated a diminished TSH concentration among individuals diagnosed with COVID-19. This phenomenon can be elucidated through two theoretical frameworks [27]. The first posits that there is direct impairment of the follicular tissue by the SARS-CoV-2 virus. However, this assertion was challenged by an alternative investigation which suggested that pituitary dysfunction occurs rather than destruction of the thyroid tissue [28]. In a separate cohort study, Zhang and colleagues reported the presence of thyroid abnormalities in 28% of 71 COVID-19 patients, predominantly characterized by non-thyroidal illness syndrome (48%) and subclinical hypothyroidism (28%) [29]. Similarly, Gao et al. examined 100 COVID-19 patients (66% of whom were classified as severely or critically ill). They demonstrated that the levels of fT3, TSH, and the fT3/fT4 ratio declined in conjunction with clinical deterioration, notably lower in non-survivors. Furthermore, the reduction in fT3 concentrations was found to be independently correlated with all-cause mortality [30]. Consequently, our study corroborates earlier findings regarding the significant presence of thyroid dysfunction in patients afflicted with COVID-19.

This investigation encountered several methodological limitations. Firstly, there was a relatively small sample size of consenting participants and no follow-up duration. Secondly, the assessment of free T3, free T4, and additional pituitary hormones was not conducted at either the time of admission or during follow-up, attributable to the study's cross-sectional design. Given that our institution functions as a tertiary care facility, it encountered a preponderance of cases classified as moderately severe or greater in terms of COVID-19 severity. Consequently, individuals presenting with mild COVID-19 symptoms were not evaluated for thyroid function.

5. Conclusion

Patients with COVID-19 are liable to develop thyroid function abnormalities that may explain several of the long-term symptoms associated with the disease.

Recommendation

A larger sample size from different Iraqi governorates is required to assess the effect of the COVID-19 virus infection on thyroid function.

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Data Availability

All relevant data are upon request.

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