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THYROID DISORDERS INFLUENCE THE CLINICAL SEVERITY OF COVID-19: A COMPREHENSIVE ANALYSIS

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Abstract

*P The objective of this study was to evaluate the predictive impact of thyroid gland diseases on the clinical severity of COVID-19. **Study Design**: A prospective study was conducted at Khyber Medical University (KMU) from January 2021 to November 2021. A total of 150 patients of both genders, aged 25-80 years, were included. All participants provided informed consent for the collection of detailed demographic information, including age, gender, body mass index (BMI), residency, educational and socio-economic status. Each patient underwent PCR testing to confirm COVID-19 infection. Patients were divided into two groups: Group I (75 symptomatic) and Group II (75 asymptomatic). Blood samples were tested for thyroid-stimulating hormone (TSH), free thyroxine (FT4), free triiodothyronine (FT3), thyroid peroxidase antibodies, and thyroglobulin antibodies. Data analysis was performed using SPSS 22.0. **Results**: The study included 90 male patients (45 in each group) and 60 females. The mean age of Group I was 51.32 ± 4.19 years, with a BMI of 26.13 ± 13.23 kg/m², while Group II had a mean age of 49.45 ± 23.77 years and a BMI of 25.11 ± 9.44 kg/m². In Group I, 32 (42.7%) were from urban areas, 29 (38.9%) were literate, and 52 (69.3%) had a poor socio-economic status. In Group II, 35 (46.7%) were urban dwellers, 33 (44%) were educated, and 49 (65.3%) had a poor socio-economic status. Among Group I patients, 43 (57.3%) had severe disease, whereas only 18 (24%) of Group II had severe symptoms. Group I patients exhibited significantly lower blood levels of FT4 and FT3 compared to Group II. Overt thyroid disorders were significantly more common in Group I (9 patients, 12%) than in Group II (4 patients, 5.3%). Group I had 18 (24%) cases of thyroid nodules >1 cm, while Group II had 8 (10.7%) cases. Mortality rates were significantly higher in Group I ($p < 0.05$). The study concluded that thyroid hormone abnormalities were more prevalent in patients with severe COVID-19. FT3 levels at the time of hospital admission could serve as a prognostic indicator in COVID-19 patients, and thyroid nodules may be associated with the severity of the disease.*

INTRODUCTION

Coronavirus disease 2019 (COVID-19) has become a worldwide burden, affecting individuals of all ages because of the increasing number of cases and the rapid evolution of SARS-CoV-2 [1.]. For this present outbreak of COVID-19, identifying risk indicators that may forecast the patients' outcomes is essential for a more efficient use of resources in minimizing the disease's existing symptoms and severity. [2]

Coughing or exhaling can spread COVID 19 respiratory droplets to healthy people, who can then become infected. Dry cough and fever are among COVID-19's most common

symptoms. Small and progressive symptoms are usually the norm here. Around 80 percent of people recover from the disease without needing any specific treatment or intervention.. Those over the age of 65 and those with underlying conditions such as hypertension, cardiac issues, or diabetes are more likely to have COPD advance to a more severe form [3].

There was a high prevalence of diabetes, hypertension, coronary heart disease, and stroke in COVID-19 patients [4, 5]. Additionally, diabetes types 1 and 2 may increase the risk of developing COVID-19 due to immunologic dysfunction [5, 6]. As a result, it isn't clear if COVID-19 and thyroid problems are linked in any way.

COVID-19 has been linked to a number of long-term effects on the body's natural physiological balance, which is currently affecting people worldwide. At an alarming rate, researchers are uncovering the complexities and severity of human organ systems such as the respiratory and digestive, circulatory and immune, renal and hepatocellular. COVID-19's impact on human thyroid function is becoming more widely known, which is helping us better understand thyroid dysfunction and the underlying mechanisms. Note that the thyroid gland expresses both ACE2 and transmembrane peptidase serine 2 (TMPRESS2) at high levels, which is even higher than that reported in lungs. ACE2 and TMPRS2 must be present in order for the virus to enter human cells.[7,8]

Interleukin-6 is released after an excessive immune response caused by COVID-19's disruption of desiodases and thyroid transport proteins (IL-6). Thyroid dysfunction is the obvious effect. T3 levels have a negative correlation with IL-6, in addition to a decrease in TSH and T4. One of the most common terms used to describe this situation is sick euthyroid syndrome [9]. In the course of COVID-19 pneumonia, graves or subacute inflammatory thyroiditis may cause thyrotoxicosis to develop. This can be exacerbated by arrhythmias and thromboembolic events COVID-19 [10] should be used to evaluate anomalies related with thyroid dysfunction.More and more studies are looking into whether COVID-19 patients with thyroid issues have a higher risk of complications. Hypothyroidism had no effect on the outcome of COVID-19 patients in a New York City retrospective study [11]. A meta-analysis of observational studies found that COVID-19 patients with prior thyroid issues had worse outcomes [12], but the study selection techniques and the small number of patients may have had an impact on this finding. [12]

As part of this study, patients with COVID19 who had nodules were compared to those who did not have any thyroid nodules.

MATERIAL AND METHODS

This prospective study was conducted at in Khyber Medical University (KMU) from Jan 2021-November 2021 and comprised of 150 patients had coronavirus infection. All patients signed a consent form indicating their agreement to have their demographic data collected, including their age, gender, BMI, place of residence, level of education, and overall socioeconomic status. Patients with cardiac failure, kidney failure and those did not provide any written consent were not included in this study.

A real-time reverse transcription polymerase chain reaction (RTPCR) on samples taken from the patient's nose and throat confirmed that the patient had COVID19, regardless of the test results from the nasopharyngeal swab.

The first morning of a patient's stay in the hospital, fasting blood samples were taken as per standard procedure. Glucose (urea), creatinine, AST, ALT, albumin, ferritin, C-reactive protein (CRP), D-dimer, and thyroid stimulating hormone were all measured as part of a full blood count as a precaution. In order to classify the thyroid hormone readings from patients, the following definitions were used. TSH levels were found to be significantly lower than the reference ranges for both overt and subclinical thyrotoxicosis in this study. If a patient's TSH and/or FT4 and/FT3 serum levels fell outside of the recommended reference ranges, it was considered overt hypothyroidism. Low or high

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TSH levels in the presence of FT4 and FT3 levels within the respective reference ranges were considered to indicate subclinical thyroid impairment.Patients were categorized into two equal groups, I and II. 75 symptomatic patients were included in group I and group II had 75 asymptomatic cases.

We used SPSS 22.0 edition to analyze complete data. We used standard deviation, frequencies and percentages for categorical variables.

RESULTS

Ninety (90) patients (45 in each group) were males and the rest 60 patients were females. 51.32 ± 4.19 years was the mean age in group I with mean body mass index26.13±13.23 kg/m^2 and in group II mean age was 49.45±23.77 years with mean BMI 25.11±9.44 kg/m^2. 32 (42.7%) and 35 (46.7%) cases had urban residency in group I and II. Twenty nine (38.9%) patients were literate in group I and in group II 33 (44%) cases were educated. Majority of the patients among both groups had poor socio-economic status 52 (69.3%) and 49 (65.3%).(table 1).

Table 1: Characteristics details of enrolled cases

Variables	Group I	Group II
Mean age (years)	51.32 ± 4.19	49.45±23.77
Mean BMI (kg/m^2)	26.13±13.23	25.11±9.44
Sex		
Men	45 (60%)	45 (60%)
Women	30 (40%)	30 (40%)
Residency		
Urban	32 (42.7%)	35 (46.7%)
Rural	43 (57.3%)	40 (53.3%)
Education Status		
Educated	29 (38.9%)	33 (44%)
Non-educated	46 (61.1%)	42 (56%)
Socio-economic status		
Poor	52 (69.3%)	49 (65.3%)
Good	23 (30.7%)	26 (34.7%)

In group I majority of the patients 43 (57.3%) cases had severity of disease and in group II 18 (24%) patients had severe infection.(table 2).

Table 2: Comparison of severity of disease among enrolled cases

Variables	Group I	Group II
Chronic COVID-19		
Yes	43 (57.3%)	18 (24%)
No	32 (42.7%)	57 (76%)

Comparing the results of group I patients to those of group II, it was found that group I patients had considerably lower blood levels of free thyroxine (FT4) as well as blood levels of free triiodothyronine (FT3).When comparing groups I and II, IL-6 levels were considerably higher in group I.(table 3).

Table 3: Thyroid function was compared between the two groups

Variables	Group I	Group II
Thyroid function		
TSH (mIU/L)	2.11 ±3.11	3.12±6.33
FT4 (mcg/dL)	6.15±6.23	9.04±3.27
FT3 (ng/dL)	76.33±9.44	113.5±8.36
IL-6 (pg/mL)	17.5±6.22	8.9±13.31

Frequency of overt thyroid disorder was significantly higher in group I found in 9 (12%) as compared to group II 4 (5.3%). We found 18 (24%) cases in group I had thyroid nodules size>1cm while in group II 8 (10.7%) had nodule size >1cm.(table 4)

Table 4: Association of thyroid disorders among both groups

Variables	Group I	Group II
Overt thyroid disorder		
Yes	9 (12%)	4 (5.3%)
No	66 (88%)	71 (94.7%)

Thyroid nodules size		
>1cm	18 (24%)	8 (10.7%)
<1cm	57 (76%)	67 (89.3%)

Mortality in group I was significantly higher with p value <0.05.(table 5)

Table 5: Mortality in group I and in group II

Variables	Group I	Group II
Mortality		
Yes	19 (25.3%)	7 (9.3%)
No	54 (74.7%)	68 (91.7%)

DISCUSSION

Thyroid disorders can have long-term consequences, including heart and respiratory system functions as well as catabolism. This is why many low-income countries have implemented salt iodination to combat the effects of iodine-deficient thyroid disorders[13, 14]. Over a million people in developing and middle-income countries have already died as a result of a new disease known as COVID-19, and the death toll continues to rise. [15,16]In this prospective study 150 patients had coronavirus disease with ages 25-80 years were included. There were majority males 60% with age 51 years.[17] In the presented patients 58.7% had poor socioeconomic status and 41.3% patients were educated. Previous research presented same results to our studies.[18]

Patients with critical COVID-19 symptoms had lower TSH levels than those without symptoms, according to our findings. Furthermore, patients with COVID-19 had significantly elevated TT3 levels at follow-up with little or no effect on TT4 levels. This complicates things further. While hypothyroidism affects 4.1 percent of the population in Pakistan, hyperthyroidism and subclinical hyperthyroidism affect 5.1 and 5.8 percent of the population, respectively. [20] Despite the fact that hyperthyroidism is a rare illness in Pakistan. However, our prevalence appears to be far greater than the prevalence of both disorders, which are both 0.7% in Europe and 0.5% in the United States, while the prevalence of subclinical and overt hyperthyroidism as well as hypothyroidism is comparable in our closest neighbor India at 1.6% and 1.3%, respectively. [21,22]

TSH levels were found to be lower in patients with COVID-19, according to one study. These two possibilities [23] can explain it. SARS-COV-2 can cause damage to hair follicles directly. However, another study suggested that pituitary dysfunction may be to blame instead than thyroid tissue damage. However, a condition known as sick euthyroid occurs in critically ill patients who show signs of thyroid dysfunction. A wide range of factors contribute to this syndrome, including changes in TSH production, binding to transport proteins, and uptake of thyroid hormone in the peripheral bloodstream. In patients with sick euthyroidism, therapy with thyroid hormone has little effect on this pathological response to acute sickness [24]. COVID-19's effect on ill euthyroid has been studied in several studies [25].

Frequency of overt thyroid disorder was significantly higher in group I found in 9 (12%) as compared to group II 4 (5.3%). We found 18 (24%) cases in group I had thyroid nodules size>1cm while in group II 8 (10.7%) had nodule size >1cm. The COVID-19 epidemic appears to have had little effect on Pakistan's population, compared to other countries where it has destroyed populations. When it comes to critically ill patients, the long-term consequences of COVID-19, particularly when it comes to follow-up, appear to be disregarded. An aged patient may misinterpret the symptoms of high blood levels of TT3 (such as fatigue, dizziness, and an elevated heart rate) as a result of the body's recovery from a viral illness. The signs and symptoms of both thyroid storms and cytokine storms in severely ill patients share many of the same hallmarks [30]. During the 2002 SARS epidemic, postmortem examinations of thyroid tissue from deceased patients showed a precedent for the effect of an earlier coronavirus on the thyroid.[31] This immunogenic and hormonal overlap of a distinct condition may unintentionally cause thyroid auto-immune damage when

corticosteroids are used to treat COVID-19 in group I, the p value was less than 0.05, which indicated that death rates were significantly higher.

Thyroid issues are one of the many ways COVID-19 can manifest itself. As part of the diagnosis, patients with COVID-19 may benefit from having their thyroid function evaluated. The severity of COVID-19 is correlated with low T3 syndrome prevalence in this patient population. Although the efficiency and safety of T3 supplements are still being explored, it is possible that it will improve the prognosis for seriously ill individuals. If RDV and ATDs are administered to hyperthyroidism patients in the hospital, there is an increased risk of acute liver injury. Dexamethasone and heparin may also cause a misdiagnosis of hypothyroidism, as both medicines can alter thyroid hormone production and measurement.[32]

COVID-19 people who are asymptomatic or moderately afflicted can be cared for at home. If a therapy change is needed or if signs of thyroid malfunction emerge, a thyroid function test should be performed.

CONCLUSION

This study came to the conclusion that overt thyroid hormonal abnormalities were more prevalent in severely ill COVID19 patients. It is possible that the FT3 level at the time of hospital admission is a prognostic indicator in COVID19 patients. Symptoms of severe COVID-19 disease may include thyroid nodules.

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