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**Research Paper**

# Thyroid function status in patients with COVID-19: A retrospective analysis in tertiary care level

Umakanta Mahapatra[1] Arindam Bhattacharjee[2] Rabi Lochan Maji[2] Kalimujjaman Molla[3] Kripasindhu Gantait[4]

1. *Assistant professor, Department of General Medicine, Midnapore Medical College & Hospital, Midnapore, India*
2. *Post-graduate trainee, Department of General Medicine, Midnapore Medical College & Hospital, Midnapore, India*
3. *Senior resident,Department of General Medicine, Midnapore Medical College & Hospital, Midnapore, India*
4. *Professor, Department of General Medicine, Midnapore Medical College & Hospital, Midnapore, India*

*Corresponding author: Prof Kripasindhu Gantait*

***ABSTRACT:***

***Background:*** *Infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) may affect multiple organs other than the lungs and the immune system. Recent many studies have shown thyroid function abnormalities of various types in COVID-19 cases. In this study, we aimed to evaluate the thyroid function status in COVID-19 patients.*

***Methodology:*** *Clinical manifestations, basic laboratory parameters, and thyroid function tests were retrospectively reviewed for 111 patients with laboratory-confirmed COVID-19 without a history of thyroid disease who underwent thyroid function testing during their hospital stay. Data of the patients admitted in Midnapore Medical College & Hospital from 1st September to 30th September of 2021 were collected and analyzed retrospectively.*

***Results:*** *Among the total 111 patients, 64(57.65%) were male, and 47(42.35%) were female. In this study total number of patients (111) are divided into two groups, severe group (59 patients) and mild group (52 patients). Further among the severely ill patients are divided into two groups according to the final outcome, the non-survivor group having 21 and the survivor group having 38 patients. In the study, we found the common symptoms of presentation were – fever (90.38% in the mild group and 62.71% in the severe group), dyspnoea (93.22% in the severe group), and cough (73.07% in the mild group and 71.18% in severe group). The patients in the severe group had significantly lower SBP on presentation, higher Respiratory rate(RR), and lower SpO2 than patients of the mild group ($p<0.05$). Total leukocyte count (TLC), NLR, C-reactive protein(CRP), D-dimer, Urea, and Creatinine were significantly increased in patients of the severe group compared to the mild ($P<0.05$). Among the severe group, patients of the non-survivor group were significantly older, more hypoxic, more tachypneic, had significantly higher TLC, NLR, Urea, Creatinine, CRP, and D-dimer than the survivor group (p-value <0.05). This study has revealed that among patients with COVID-19, TSH and FT4, and FT3 were lower in the Severe group than the mild group and were further lower in patients who died. Low FT3 was the commonest thyroid function abnormality found in the study. FT3 was significantly lower in the severe group than the mild group ($p<0.05$), and also, a lower FT3 level was found to be significantly associated with the risk of mortality.*

***Conclusion:*** *Thyroid function may be abnormal in all categories of patients during COVID‑19 infection, even in the absence of pre‑existing thyroid illness. Low FT3 is significantly associated with severity and mortality in patients with COVID-19.*

***Keywords:*** *COVID-19, Survivor, Non-survivor, TSH, FT4, FT3.*

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## I. INTRODUCTION:

The Coronavirus infection emerged on a large scale from Wuhan and spread all over the world in January 2020 and is now known to be transmitted by person-to-person contact. The disease caused by SARS-CoV- 2 infections is called coronavirus disease 2019 (COVID- 19) by WHO, and the COVID-19 pandemic was declared as a public health emergency of international concern on 30th January 2020[1]. Clinical symptoms are mainly characterized by fever, dry cough, sore throat, anorexia, etc. A small number of patients will have dyspnoea, muscle soreness, and other symptoms, and severe patients may progress to acute respiratory distress signs, sepsis,coagulation disorders, and multiple organ failure, or even death[2]. Literature on COVID-19 affecting human thyroid function is increasing gradually, and the understanding of thyroid dysfunction and its mechanism is growing. The expression of ACE2 combined with trans-membrane protease serine 2 (TMPRESS2) is the key cellular complex for the virus to infect the human cells, and interestingly both expression levels are present in the thyroid gland, even more than in the lungs[3]. In this retrospective study, we aimed to compare the characteristics of thyroid function between mild and severely ill covid-19 patients and its role in predicting the risk of mortality in severely or critically ill patients with COVID-19.

## II. MATERIALS AND METHODS:

**Study population:**

We chose 129 patients diagnosed with COVID-19 admitted to Midnapore Medical College & Hospital, Paschim Medinipur, West Bengal, from 1st September to 30th September of 2021. Patients were admitted in MATANGINI HAZRA WARD and SARI HDU, which had been deputed for managing mild and severe covid-19 patients, respectively. This categorization of covid-19 patients was done according to the existing government protocol. Of these, twelve were excluded due to the lack of laboratory test results, and six patients were excluded because of having hypothyroidism. Finally, 111 patients were included in our study. The general clinical characteristics of the patients were collected, including age, gender, clinical symptoms, basic laboratory investigations, and thyroid function test, including TSH, FT4, and FT3. All the data were collected from the BHTs (bed head tickets) in the record section.

**Study design and Laboratory Investigations:**

In this retrospective, single-centered and observational study conducted at Midnapore Medical College and Hospital, Paschim Medinipur, West Bengal, India, from 1$^{st}$ September 2021 to 30$^{th}$ September 2021, written informed consent was waived by the Institutional Research Committee of Midnapore Medical College and Hospital. We included adult patients (>18 years old) with confirmed severe COVID-19 (diagnosed using RT-PCR assay) infection, and we excluded patients having any pre-existing thyroid disorder. We have divided all the patients with COVID-19 into two groups, Non-severe and Severe, defined as per existing Govt. guidelines. Severe illness was defined as patients with COVID-19 with blood oxygen saturation $\leq 93\%$ or respiratory rate $\geq$ 30 per/min on admission[4] or patients with COVID-19 who were complicated by ARDS, sepsis shock, and/or organ failure, including acute heart failure and acute kidney injury (AKI) or ongoing hemodialysis during the hospital stay. Patients with COVID-19 who had only pneumonia without the above conditions were classified as non-severe illness

Clinical data includes demographic information (age, gender, date of admission, date of discharge, co-morbidities), medical history, laboratory tests (routine blood tests and thyroid function test), and outcomes (death and survivor).

**Statistical analysis:**

This study's data were coded and analyzed using Statistical Package for Social Sciences (SPSS) version 28. Quantitative data of normal distribution were expressed as mean ± SD ($x \pm s$), and independent-sample t-test was used for comparison between groups; categorical data were expressed by percentage (%), and Pearson chi-square test or Fisher's exact test was used for comparison, $p < 0.05$ was considered statistically significant.

## III. RESULTS:

In this study total number of patients (111) are divided into two groups, severe group(59) and mild group(52). Further among the severely ill patients are divided into two groups according to the final outcome, the non-survivor group having 21 and the survivor group having 38 patients. The mean age of the severe group and the mild group were 61.80±11.14 and 42.48±9.07, respectively, and the difference was statistically significant ($p<0.05$). Among the total 111 patients, 64 were male, and 47 were female. Dyspnoea was the most common mode of presentation in the severe group (93.22%), followed by cough (71.18%) and fever (62.71%). In the mild group, fever (90.38%) was the most common clinical manifestation, followed by cough (73.07%) and sore throat (32.69%). Other modes of presentation were anorexia, headache, and chest pain (table 1).

| Variables | Severe (n=59) | Mild (n=52) | p-value | Non-survivor (n=21) | Survivor (n=38) | p value |
|---|---|---|---|---|---|---|
| **Age** | 61.80±11.14 | 42.48±9.07 | <0.05 | 70.33±8.74 | 57.08±9.43% | **<0.05** |
| **Sex** | Male-35 Female-24 | Male-29 Female-23 | - | Male-11 Female-10 | Male-24 Female-14 | - |
| **Dyspnoea** | 55(93.22%) | 1(1.92%) | <0.05 | 18(88.71%) | 37(97.36%) | 0.12 |
| **Cough** | 42(71.18%) | 38(73.07%) | 0.83 | 17(80.95%) | 25(65.78%) | 0.24 |
| **Fever** | 37(62.71%) | 47(90.38%) | <0.05 | 12(57.14%) | 25(65.78%) | 0.58 |
| **Anorexia** | 12(20.33%) | 5(9.61%) | 0.18 | 6(28.57%) | 6(15.78%) | 0.31 |
| **Headache** | 0 | 8(15.38%) | <0.05 | 0 | 0 | - |
| **Chest pain** | 3(5%) | 0 | 0.24 | 0 | 3(7.89%) | 0.54 |
| **Sore throat** | 0 | 17(32.69%) | <0.05 | 0 | 0 | - |

**Table 1: Clinical presentations of 111 covid-19 patients by severity and survival status**

In this study, we found patients in the severe group were more hypoxic (mean Spo2 78.34±6.07) than the mild group (mean Spo2 95.79±1.87), and more tachypnoea was seen in the severe group (mean RR, 32.86±4.67) than the mild group (mean RR, 17.92±2.93). Mean systolic blood pressure on admission was lower in the severe group (107.69±19.78) than in the mild group (122.73±14.86). All of these differences were statistically significant (p-value <0.05). In our study, we found total leukocyte count(TLC), Neutrophil-to-lymphocyte ratio (NLR), Urea, Creatinine, C-reactive protein(CRP), and d-dimer were significantly higher in the severe group compared to the mild group; the differences were statistically significant ($p < 0.05$). When we compared thyroid function between the severe and mild groups, we found the level of TSH, FT4, and FT3 were significantly lower in the severe group than in the mild group (p value<0.05). We also found that the patients who died were more hypoxic, tachypneic, had higher TLC, NLR, Urea, Creatinine, CRP, and D-dimer than the patients who survived (p-value <0.05). Regarding thyroid function, we found low FT3 (normal range 2.6-4.4 pg/ml) was the commonest thyroid abnormality (61 patients, 54.95%). The level of TSH and FT4werefound to be significantly lower in severe covid-19 patients than patients of the mild group (p<0.05). Further, TSH and FT4 were found to be significantly lower in the non-survivor group than survivor (p<0.05).FT3 level was found to be lower in the severe group than the mild group, and the difference was statistically significant (p <0.05). Also, mean FT3 was lower in the non-survivor group than survivor group, and it was found to be statistically significant (p<0.05) (table 2).

| Variables | Severe (n=59) | Mild (n=52) | p-value | Non-survivor (n=21) | Survivor (n=38) | p-value |
|---|---|---|---|---|---|---|
| **SBP** | 107.69±19.78 | 122.73±14.86 | **<0.05** | 102.48±17.60 | 110.58±20.54 | 0.13 |
| **SpO2** | 78.34±6.07 | 95.79±1.87 | **<0.05** | 74.57±5.51 | 80.42±5.36 | **<0.05** |
| **RR** | 32.86±4.67 | 17.92±2.93 | **<0.05** | 34.76±3.49 | 31.82±4.94 | **<0.05** |
| **TLC** | 15.93±3.34 | 7.39±1.84 | **<0.05** | 18.32±2.39 | 14.60±3.06 | **<0.05** |
| **NLR** | 4.66±0.83 | 3±0.55 | **<0.05** | 5.01±1.03 | 4.46±0.63 | **<0.05** |
| **Urea** | 56.24±13.85 | 31.77±5.42 | **<0.05** | 67.71±14.82 | 49.89±8.11 | **<0.05** |
| **Creatinine** | 1.55±.51 | 0.93±0.13 | **<0.05** | 1.83±0.46 | 1.41±0.30 | **<0.05** |
| **CRP** | 78.37±26.62 | 14.13±5.76 | **<0.05** | 103.38±16.41 | 64.55±20.35 | **<0.05** |
| **D-Dimer** | 3906±142 | 502±279 | **<0.05** | 4952±821 | 3328±1071 | **<0.05** |
| **TSH** | 1.76±1.37 | 3.55±0.75 | **<0.05** | 2.27±1.75 | 1.48±1.02 | **<0.05** |
| **FT4** | 1.10±0.35 | 1.38±0.19 | **<0.05** | 0.92±0.25 | 1.19±0.36 | **<0.05** |
| **FT3** | 1.38±0.41 | 3.34±0.59 | **<0.05** | 1.21±0.28 | 1.48±0.44 | **<0.05** |

**Table 2: Vital signs, basic laboratory parameters, and thyroid function test of 111 covid-19 patients by severity and survival status**

## IV. DISCUSSION:

In this study, we included 111 patients with RT-PCR confirmed covid-19. Among them, 64 were male (57.65%), and 47 were female (42.35%). Patients of the severe group were older (mean age 61.80±11.14) than the mild group (mean age 42.48±9.07)[5]. In this study, common symptoms of presentation were – fever (90.38% in the mild group and 62.71% in the severe group), dyspnoea (93.22% in the severe group), and cough (73.07% in the mild group and 71.18% in severe group). Other modes of clinical presentation were sore throat, headache, anorexia, and chest pain[6]. Dyspnoea was the most common presenting complaint in severe patients and fever in patients of mild group.

In our study, we found patients in the severe group had significantly lower SBP on presentation, higher Respiratory rate(RR), and lower SpO2 than patients of the mild group (p<0.05). Total leukocyte count (TLC), NLR,C-reactive protein(CRP), and D-dimer were significantly increased in patients of the severe group compared to the mild (P <0.05), and previous studies also had shown similar results[7][8]. Many previous studies have identified acute kidney injury (increased urea and creatinine) as a sequela frequently present in the Covid-19 patients with severe disease, many of whom expired[9]. In our study, urea and creatinine were significantly higher in the severe group compared to the mild group (p value< 0.05).

In this study, we again divided the patients of the severe group based on the final outcome into two groups, survivor (21 patients, 35.59%) and non-survivor (38 patients, 64.41%). All the patients who died (21) were in the severe group. Patients who died were older than patients of the survivor group, and the difference was statistically significant (p-value <0.05). Patients of the non-survivor group were significantly more hypoxic, more tachypneic, had significantly higher TLC, NLR, Urea, Creatinine, CRP, and D-dimer than the survivor group (p-value <0.05).

Although in COVID-19 patients, the lung is the key lesioned organ, angiotensin-converting enzyme 2 (ACE2), the receptor for SARS-CoV-2 to invade humans, is expressed at a high level in the thyroid [10]. A previous study reported that the thyroid glands of patients with SARS were significantly affected by extensive injury to the follicular epithelial and Para follicular cells [11]. Another previous study showed that the TT3, TT4, and TSH levels of patients with SARS were considerably lower than those of controls in both the progression and re- recovery phases [12]. The results of our study showed that among patients with COVID-19, TSH and FT4 and FT3 were lower with clinical deterioration of COVID-19 and were further lower in patients who died. Some previous studies have shown similar results [13][14]. Low FT3 was the commonest thyroid function abnormality found in the study. Some previous studies showed that the mortality rate of patients with normal TSH was lower than that of patients with abnormal TSH[15][16]. In our study, FT3 was significantly lower in the severe group than the mild group(p <0.05), and also, a lower FT3 level was found to be significantly associated with the risk of mortality. Some previous studies have shown lower FT3 is associated with increased severity and mortality in covid-19 patients [17][18].

## V. CONCLUSION:

Thyroid function may be abnormal in all categories of patients during COVID‐ 19 infection, even in the absence of pre‐ existing thyroid ailments. FT3 is significantly low in patients with severe COVID-19 than non-severely ill patients and also an important risk factor of mortality in patients of COVID-19.

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