Clinical Case Reports: Open Access

Yumed Text
OPEN ACCESS JOURNALS

Case Series | Vol 7 Iss 1
ISSN: 2582-5038
https://dx.doi.org/10.46527/2582-5038.292

# Unraveling the Enigma: Subacute Thyroiditis Unleashed by the Pandemic - A Captivating COVID-19 Case Series

**Saurabh Arora, Manjeet Kumar Goyal*, Ashita Rukmini Vuthualuru, Suhani FNU, Kanwarpal Kaur Dhaliwal and Amanpreet Singh**

Gastroenterology, All India Institute of Medical Sciences, New Delhi, India

***Corresponding author:** Goyal MK, IBD Fellow, DM Gastroenterology, MBBS, MD Internal Medicine, DNB Internal Medicine, All India Institute of Medical Sciences, New Delhi-110029, India, Telephone: +91-8285234620; E-mail: manjeetgoyal@gmail.com

**Received:** March 09, 2024; **Accepted:** March 24, 2024; **Published:** March 31, 2024

## Abstract

**Sub-acute thyroiditis is an inflammatory condition of the thyroid gland, often attributed to viral infections. The novel coronavirus, SARS-CoV-2, has been associated with various endocrine manifestations, including thyroid dysfunction. This case series presents five patients with sub-acute thyroiditis following COVID-19 infection. Clinical, laboratory, and imaging findings were analyzed to assess the characteristics of this condition. Five patients, three females and two males, aged between 34 and 87 years, developed sub-acute thyroiditis within 1 to 4 weeks after COVID-19 infection. They presented with symptoms such as neck pain, fever, fatigue, and thyrotoxicosis. Thyroid function tests showed elevated thyroid hormones and suppressed thyroid-stimulating hormone (TSH) levels. Thyroid ultrasound revealed diffuse or focal thyroid gland inflammation with reduced echogenicity. All patients responded well to nonsteroidal anti-inflammatory drugs (NSAIDs) and beta-blockers, and thyroid function normalized within a few weeks. Sub-acute thyroiditis may be a rare but significant endocrine manifestation following COVID-19 infection. Clinicians should be aware of this condition in patients presenting with neck pain and thyrotoxicosis after recovering from COVID-19. Early diagnosis and appropriate management can lead to a favorable outcome. this case series delves into clinical profiles, diagnostic workup, treatment modalities, and outcomes of the five cases, thereby contributing to our understanding of this intriguing intersection between COVID-19 and endocrine health.**

## 1. Introduction

The COVID-19 pandemic has unfolded as an unprecedented global health crisis, with its clinical manifestations spanning a wide spectrum. As we continue to decipher the multifaceted nature of the novel coronavirus, SARS-CoV-2, it becomes

**Citation:** Arora S, Goyal MK, Vuthualuru AR, et al. Unraveling the Enigma: Subacute Thyroiditis Unleashed by the Pandemic - A Captivating COVID-19 Case Series. Clin Case Rep Open Access. 2024;7(1):292.

increasingly evident that its impact extends beyond respiratory symptoms [1]. Emerging evidence suggests that COVID-19 can affect various organ systems, including the endocrine system. Among these endocrine manifestations, sub-acute thyroiditis has garnered attention as a noteworthy clinical entity [2].

Sub-acute thyroiditis, also known as de Quervain's thyroiditis, is an inflammatory disorder of the thyroid gland characterized by painful swelling of the neck, fever, and transient thyrotoxicosis. It is typically triggered by viral infections, though various viruses have been implicated as causative agents. With the global prevalence of COVID-19, healthcare professionals have witnessed an array of associated complications, some of which, like sub-acute thyroiditis, are beginning to come to the forefront [3].

The link between COVID-19 and thyroid dysfunction has been an intriguing area of research and clinical observation. This case series aims to shed light on the occurrence of sub-acute thyroiditis in the aftermath of COVID-19 infection. In this series of five cases, we present a comprehensive overview of the clinical characteristics, laboratory findings, and management of patients who developed sub-acute thyroiditis in the wake of recovering from COVID-19. By elucidating the nuances of this endocrine manifestation, we contribute to the growing body of knowledge concerning the wide-ranging impact of the SARS-CoV-2 virus [4].

Understanding the relationship between COVID-19 and sub-acute thyroiditis not only expands our comprehension of the virus's pathophysiology but also underscores the importance of vigilant clinical evaluation and management of individuals with post-COVID-19 complications [4]. This case series underscores the need for clinicians to consider sub-acute thyroiditis as a potential sequela in patients presenting with neck pain and thyrotoxicosis in the post-COVID-19 period, facilitating timely diagnosis and appropriate therapeutic interventions.

In this case series, we delve into the clinical profiles of the five cases, their diagnostic workup, treatment modalities, and outcomes, thereby contributing to our understanding of this intriguing intersection between COVID-19 and endocrine health.

## 2. Case Presentation

### 2.1 Case 1

A 34-year-old woman presented with a 22-day history of fever, dry cough, and sore throat. She had a temperature of 104.6°F, blood pressure of 116/80 mm Hg, heart rate of 86 beats/min, respiratory rate of 14 breaths/min, and an oxygen saturation (SpO2) of 97% on room air. Auscultation of the lungs was clear with no added sounds. Reverse transcription-polymerase chain reaction for SARS-CoV-2 using nasopharyngeal swab was positive. Initial laboratory results revealed a normal white cell count (8.8 × 109/L), hemoglobin level (12.5 g/dL), and platelet count (2,48 000/mm3). C reactive protein (CRP) level was 31.3 mg/L, and lactate dehydrogenase (LDH) was within normal limits at 342 units/L. A chest X-ray (CXR) showed no evidence of pulmonary infiltrates or consolidation. The patient was managed symptomatically without glucocorticoids and was advised for home isolation in view of normal oxygen saturation.

On day 7, she was afebrile with SpO2 of 98% on room air and CRP was 40 mg/L. Her leucocyte count was within normal limits, and she was advised for home isolation. On day 14 of illness, she again started having continuous fever. On examination, she had a heart rate of 106/ min and SpO2 of 98% on room air. A neck examination revealed few cervical lymph nodes palpable bilaterally. The Chest examination was normal. Her leucocyte count was normal, but CRP increased to 152.99 mg/L. Her erythrocyte sedimentation rate (ESR) was 92 mm/hr. Serum Ferritin, LDH, and D-dimer were within the reference range. Repeat chest x-ray showed no evidence of infiltrates, consolidation, and pleural effusion. The possibility of cytokine storm was less likely in view of normal SpO2, ferritin, and chest x-ray. Thyroid function test revealed high free T3 (9.38pg/ml), high free T4(3.31 ng/dl), and suppressed TSH(0.026 µIU/ml). Thyrotropin receptor antibody (TRAb) and thyroperoxidase antibody (TPOAb) were negative. ECG revealed sinus tachycardia and procalcitonin was normal.

She was started on 20 mg prednisolone and propanolol 40 mg per day. Two days after starting glucocorticoids, the patient became afebrile. On day 17, the patient tested negative for SARS-CoV-2 PCR and was subjected to a technetium thyroid scan. The diagnosis of subacute thyroiditis was confirmed by absent uptake on technetium 99m pertechnetate scan. She became afebrile two days after starting glucocorticoids. CRP decreased to 13.23 mg/L after 5 days of glucocorticoids and ESR decreased to 50 mm/hr. Prednisolone was tapered and stopped after 1 month. The patient remained asymptomatic after the discontinuation of glucocorticoids. At 8 weeks, her thyroid function tests normalized with a free T4 level of 1.3 ng/dl and a TSH level of µIU/ml.

### 2.2 Case 2

A 46-year-old woman presented to the hospital with complaints of anterior neck pain radiating to the right jaw and low-grade fever for 3 days. She also complained of difficulty in swallowing. She did not complain of anosmia, loss of taste, palpitations, tremors, rashes, or any upper or lower respiratory tract-related complaints. She denied any past history of thyroid disease, hypertension, and diabetes. She also complained of an increased frequency of stools. On examination, she was febrile (temperature-99.9°F) with a pulse rate of 108 beats/min. Her blood pressure was 134/84 mm Hg, respiratory rate 16/min, and oxygen saturation 98% on room air. A neck examination revealed a diffusely enlarged thyroid gland with a normal surface temperature and firm consistency, without any palpable nodules. Cervical lymph nodes were not enlarged. Systemic examination was normal.

Her laboratory investigations revealed normal white cell count (9.2 × 109/L), hemoglobin level (13.7 g/dL), and platelet count (3,56 000/mm3). C reactive protein (CRP) level was 32.4 mg/L and ESR was 82 mm/hr. Chest x-ray showed no evidence of infiltrates, consolidation, and pleural effusion. ECG showed sinus tachycardia. Thyroid function test revealed high free T3 (8.56 mol/l), high free T4 (32.9 pmol/l), and suppressed TSH (0.05 µIU/ml). Thyrotropin receptor antibody (TRAb) and thyroperoxidase antibody (TPOAb) were negative. Ultrasonography of the thyroid showed bilaterally bulky thyroid lobes with large hypoechoic areas within them. Reverse transcription-polymerase chain reaction for SARS-CoV-2 using nasopharyngeal swab turned out to be positive, thus establishing the diagnosis of subacute thyroiditis possibly related to COVID-19 infection. The diagnosis of subacute thyroiditis was confirmed by reduced uptake on technetium 99m pertechnetate scan. She was started on 20 mg prednisolone and 40 mg propranolol per day. The dose of prednisolone was gradually tapered once the patient became

asymptomatic and stopped over a period of a month. The thyroid profile repeated after 10 weeks showed normalization of T3, T4, and TSH.

### 2.3 Case 3

A 40-year-old man was admitted for evaluation of pyrexia of unknown origin. He had 23 days history of fever. He had no accompanying cough, sore throat, sweat, breathlessness, and weight loss. He had a past history of type 2 diabetes mellitus for which he was on oral hypoglycemic agents. He reported worsening of glycemic control over the last 2-3 weeks. He denied any history of neck pain, palpitations, increased frequency of stools, and tremors. General physical examination and systemic examination were within normal limits. Investigations revealed normal leucocyte count (7.6 × 109/L), hemoglobin level (13.9 g/dL), and platelet count (3,10, 000/mm3). His C reactive protein (CRP) level was 44.8 mg/Land ESR was 96 mm/hr. His workup for tropical fever, tuberculosis, and brucella was negative. RT PCR for SARS-CoV-2 turned out to be negative. Chest x-ray and computed tomography (CT) scan of chest and abdomen was normal. Thyroid function test revealed high free T3 (7.96pmol/l), high free T4 (29.42 pmol/l), and suppressed TSH (0.04 µIU/ml). Thyrotropin receptor antibody (TRAb) and thyroperoxidase antibody (TPOAb) were negative. Technetium 99m pertechnetate scan of the thyroid gland revealed absent uptake. IgM antibody against SARS-CoV-2 turned out to be positive while IgG SARS-CoV-2 antibody was negative. There was no history of COVID-19 vaccination.

The possibility of subacute thyroiditis, likely due to COVID 19 was kept and he was started on 20 mg once daily prednisolone and propanalol 40 mg per day. Fever persisted after 5 days of intake of glucocorticoids. In view of the persisting fever, the whole-body positron emission tomography CT scan was normal except for mild diffuse increased FDG uptake in the thyroid gland. The dose of prednisolone was increased to 30 mg per day. Two days after increasing the dose of glucocorticoids fever subsided and the patient was discharged. Prednisolone was gradually tapered and stopped after 6 weeks. Thyroid function test after 8 weeks revealed normal T3 and T4, but TSH increased to 32µIU/ml. He was started on levothyroxine 50 mcg once daily and regular monitoring of thyroid function tests.

### 2.4 Case 4

A 42-year-old woman diagnosed with mild COVID-19 disease presented with continuous fever for the last 2 weeks. She also complained of neck pain and palpitations for the last 3 days. General physical examination and systemic examination were within normal limits. Her oxygen saturation always remained above 95%. RT PCR for SARS-CoV-2 was positive. At 1 week, CRP was 34.2mg/L and ESR was 46 mm/hr with normal total leucocyte count. At 2 weeks, CRP increased to 103.4mg/L and ESR increased to 92 mm/hr with a leucocyte count of 12.4 × 109/L. The chest x-ray turned out to be normal. The possibility of a cytokine storm was low in view of normal oxygen saturation and normal chest x-ray. Thyroid function tests revealed elevated free T3 (8.12 pmol/l), high free T4 (31.2 pmol/l), and suppressed TSH (0.01 µIU/ml). TSH receptor antibody (TRAb) and thyroperoxidase antibody (TPOAb) were not elevated. Technetium 99m pertechnetate scan of the thyroid gland revealed absent uptake suggestive of destructive thyroiditis.

The patient was treated with 20 mg of prednisolone per day. The fever subsided within 3 days of starting glucocorticoids. The dose of prednisolone was gradually tapered and stopped after 1 month. Repeat thyroid profile at 6 weeks showed normal T3 and T4 with suppressed TSH. The patient was advised to repeat thyroid function tests after 1 month.

### 2.5 Case 5

An 87-year-old man was admitted with a history of 7 days duration of cough and sore throat. Reverse transcription-polymerase chain reaction for SARS-CoV-2 using nasopharyngeal swabs was positive. The patient denied any history of breathlessness, chest pain, palpitations, and thyroid disorder. On examination, he was febrile (temperature-99.8°F) with a pulse rate of 84 beats/min which was regular. Her blood pressure was 124/80 mm Hg, respiratory rate 16/min, and oxygen saturation 95% on room air. On the 12th day of admission, the patient had atrial fibrillation with a heart rate of 142 beats per minute and blood pressure was 106/68 mm Hg. His oxygen saturation was 95%. Electrolytes including calcium and magnesium were normal. Thyroid function tests showed increased T3 (8.8 pmol/l) and T4(28.64 pmol/l) with suppressed TSH(0.02 µIU/ml). His TPO antibody and TSH receptor antibody were negative. His CRP was 54.6 mg/L.He was started on beta blockers and glucocorticoids (dexamethasone 6 mg/day). Heart rate decreased to 88 beats/ min and blood pressure increased to 120/80 mm Hg. Technetium 99m pertechnetate scan of thyroid gland showed absent uptake consistent with a diagnosis of destructive thyroiditis. The patient was discharged on a tapering regimen of glucocorticoids and beta blockers.

## 3. Discussion

In December 2019, the World Health Organisation (WHO) was informed about cases of pneumonia in Wuhan, Hubei province, China, with an unidentified origin [5].The new virus, known as SARS-CoV-2, was discovered and isolated on January 7, 2020 [5]. The World Health Organisation (WHO) declared the acute respiratory disease, known as Coronavirus disease 2019 (COVID-19), as a pandemic on March 11, 2020.

Subacute thyroiditis, often referred to as De Quervain's thyroiditis, viral thyroiditis, subacute granulomatous thyroiditis, or giant cell thyroiditis, is an inflammatory condition of the thyroid gland that is commonly linked to or coincides with a viral infection. This is a self-resolving ailment that does not necessitate any therapy. Viral infections including mumps, measles, rubella, coxsackie, and adenovirus have been linked to the development of SAT. This might arise either from the virus's direct harmful effects or via the body's inflammatory response to the infection [6,7]. Ongoing efforts are being made to determine the endocrinological effects of COVID-19, and there have been recorded cases of abnormalities in the hypothalamic-pituitary-thyroid (HPT) axis [8]. The correlation between thyroid hormones and the immune system, together with the direct detrimental impact of the virus, is believed to be a contributing factor to these abnormalities, including subacute thyroiditis [6]. The specific mechanisms by which SARS-CoV-2 causes thyroid dysfunction are still not understood [5]. The SARS virus is associated with the following mechanisms:

1. The SARS-CoV virus triggers a strong inflammatory response in the host, leading to cell death and local tissue damage. This reaction is caused by the production of several viral proteins that induce apoptosis. A postmortem examination of 5 individuals with Severe Acute Respiratory Syndrome (SARS) conducted in 2007 revealed evidence of damage to the follicular epithelium and cellular apoptosis, without the presence of neutrophilic or lymphoid infiltration. Apoptotic cells have been detected in the liver and thyroid tissue of individuals infected with SARS-

CoV [9-13]. An inflammatory infiltration has been observed in many organs, including the thyroid, in individuals infected with SARS-CoV-2, indicating the possible involvement of inflammation.

2. Viral replication occurs directly - the viral genomes of both SARS-CoV and SARSCoV-2 have been observed in the blood of patients [14]. SARS-CoV was not found in the thyroid, but it was seen in the inflammatory cells that had infiltrated the area [15,16]. Thyroiditis has been linked to other viral illnesses due to the presence of virus-like particles in the thyroid tissue. While SARS-CoV-2 has not been definitively detected in the thyroid, the potential for direct viral harm to the organ has not been dismissed.
3. ACE2 receptor interactions - ACE2 receptors, which are present in several organs outside the lungs, such as the thyroid [17,18], play a role in these interactions. ACE2 is thought to have a vital function in the development of lung damage caused by coronaviruses [19]. Therefore, ACE2 receptors present in the thyroid gland may function as an additional means of causing harm.
4. A possible primary mechanism is that SARS patients exhibited changes in thyroid hormone levels and thyroid dysfunction [20,21]. A prior investigation indicated that reduced levels of thyroid hormones and lower levels of TSH hormones might be attributed to the pathological observations of follicular destruction [20]. Nevertheless, the decreased TSH level may be a result of a malfunction in the hypothalamus-pituitary system. This is supported by the discovery of central hypothyroidism and central hypocortisolism in individuals with SARS [21,22]. In summary, it was hypothesized that SARS-CoV might cause thyroid dysfunction through both the loss of thyroid tissue and central processes. It is uncertain if SARS-CoV-2 will exhibit comparable processes.

This article presents cases of individuals who were diagnosed with subacute thyroiditis that was triggered by a COVID-19 infection. Subacute thyroiditis, sometimes referred to as subacute granulomatous, subacute nonsuppurative, giant cell, or painful/de Quervain's thyroiditis, is a rare cause of thyrotoxicosis. Females are more commonly affected by this condition, which is generally characterized by a painful and sensitive thyroid gland. The discomfort can radiate to the ear and is accompanied by systemic symptoms such as fevers, malaise, and anorexia [7,8]. The diagnosis of subacute thyroiditis is mostly based on clinical evaluation, with laboratory tests and imaging serving as further support [7,8]. The clinical manifestations are associated with a mix of laboratory findings, including increased erythrocyte sedimentation rate and C-reactive protein levels, decreased thyroid-stimulating hormone levels, and raised levels of thyroid hormones (T4 and T3) and thyroglobulin concentrations. According to our current understanding, the literature has documented a total of 100 instances, with ages ranging from 18 to 85 years. Among these cases, 68 were women, and the most frequently seen symptom was fever. The favored therapeutic options were corticosteroids, followed by non-steroidal anti-inflammatory medications and beta-blockers [23]. All of our patients had test evidence of thyrotoxicosis and showed a positive response to treatment with anti-inflammatory and corticosteroid medications. The rapid and positive reaction to anti-inflammatory and steroid medication provides more evidence supporting our belief that COVID-19 is the underlying reason. Amidst the growing understanding of the long-term effects of COVID-19 infection, we provide instances of subacute thyroiditis resulting from SARSCoV-2 infection. Due to the widespread occurrence of COVID-19 in the population, we cannot entirely exclude the chance that our patient, who later had subacute thyroiditis, coincidentally tested positive for the SARS-CoV-2 virus. Additional investigation is required to uncover this potential connection, as well as to understand the processes behind thyroid damage and the long-term consequences.

## 4. Conclusions

The COVID-19 pandemic has led to the development of sub-acute thyroiditis, a unique clinical manifestation. This case series, involving five patients who developed the condition shortly after recovery, provides insights into the diagnostic, therapeutic, and prognostic aspects of this relationship. The study highlights the diverse clinical presentation, requiring prompt diagnosis and vigilance among healthcare providers. Early identification is crucial for preventing treatment delays and potential complications. Management strategies involve symptomatic relief and close monitoring, avoiding unnecessary thyroid hormone therapy. The findings contribute to the growing body of knowledge about the relationship between COVID-19 and endocrine health, but further research is needed to understand the exact mechanisms and identify risk factors.

## REFERENCES


1. Pollard CA, Morran MP, Nestor-Kalinoski AL. The COVID-19 pandemic: a global health crisis. Physiol Genomics. 2020;52(11):549-57.
2. Garg MK, Gopalakrishnan M, Yadav P, et al. Endocrine Involvement in COVID- 19: Mechanisms, Clinical Features, and Implications for Care. Indian J Endocrinol Metab. 2020;24(5):381-6.
3. Ando Y, Ono Y, Sano A, et al. Subacute Thyroiditis after COVID- 19: A Literature Review. Am J Trop Med Hyg. 2022;107(5):1074-82.
4. Rossetti CL, Cazarin J, Hecht F, et al. COVID-19 and thyroid function: What do we know so far? Front Endocrinol. 2022;13:1041676.
5. Khatri A, Charlap E, Kim A. Subacute Thyroiditis from COVID-19 Infection: A Case Report and Review of Literature. Eur Thyroid J. 2020;9(6):324-8.
6. Aemaz Ur Rehman M, Farooq H, Ali MM, et al. The Association of Subacute Thyroiditis with COVID-19: a Systematic Review. SN Compr Clin Med. 2021;3(7):1515-27.
7. Lazarus JH. Silent thyroiditis and subacute thyroiditis. In: Braverman LE, Utiger RD, editors. The thyroid: a fundamental and clinical text. Philadelphia. Lippincott Williams & Wilkins, USA; 1996.
8. Majety P, Hennessey JV. Acute and Subacute, and Riedel's Thyroiditis. In: Endotext. MDText.com, Inc., South Dartmouth (MA); 2000.
9. Perlman S, Dandekar AA. Immunopathogenesis of coronavirus infections: implications for SARS. Nat Rev Immunol. 2005,5(12):917-27.
10. Law PT, Wong CH, Au TC, et al. The 3a protein of severe acute respiratory syndrome-associated coronavirus induces apoptosis in Vero E6 cells. J Gen Virol. 2005,86(Pt 7):1921-30.
11. Tan YJ, Fielding BC, Goh PY, et al. Overexpression of 7a, a protein specifically encoded by the severe acute respiratory syndrome coronavirus, induces apoptosis via a caspase-dependent pathway. J Virol. 2004;78(24):14043-7.
12. Yuan X, Shan Y, Zhao Z, et al. G0/ G1 arrest and apoptosis induced by SARSCoV 3b protein in transfected cells. Virol J. 2005;2:66.
13. Chau TN, Lee KC, Yao H, et al. SARS-associated viral hepatitis caused by a novel coronavirus: report of three cases. Hepatology. 2004;39(2):302-10.

14. Chang L, Yan Y, Wang L. Coronavirus disease 2019: coronaviruses and blood safety. Transfus Med Rev. 2020;34(2):75-80.
15. Ding Y, He L, Zhang Q, et al. Organ distribution of severe acute respiratory syndrome (SARS) associated coronavirus (SARS-CoV) in SARS patients: implications for pathogenesis and virus transmission pathways. J Pathol. 2004;203(2):622-30.
16. Gu J, Gong E, Zhang B, et al. Multiple organ infection and the pathogenesis of SARS. J Exp Med. 2005;202(3):415-24.
17. Liu F, Long X, Zhang B, et al. ACE2 expression in pancreas may cause pancreatic damage after SARS-CoV-2 infection. Clin Gastroenterol Hepatol. 2020;18(9):2128-30.e2.
18. Li MY, Li L, Zhang Y, et al. Expression of the SARS-CoV-2 cell receptor gene ACE2 in a wide variety of human tissues. Infect Dis Poverty. 2020;9(1):45.
19. Kuba K, Imai Y, Rao S, et al. A crucial role of angiotensin converting enzyme 2 (ACE2) in SARS coronavirus induced lung injury. Nat Med. 2005;11(8):875-9.
20. Wang W, Ye YX, Yao H. Evaluation and observation of serum thyroid hormone and parathyroid hormone in patients with severe acute respiratory syndrome. J Chin Antituberculous Assoc. 2003;25(4):232-4.
21. Leow MK, Kwek DS, Ng AW, et al. Hypocortisolism in survivors of severe acute respiratory syndrome (SARS). Clin Endocrinol. 2005;63(2):197-202.
22. Chrousos GP, Kaltsas G. Post-SARS sickness syndrome manifestations and endocrinopathy: how, why, and so what? Clin Endocrinol. 2005;63(4):363-5.
23. Meftah E, Rahmati R, Zari Meidani F, et al. Subacute thyroiditis following COVID- 19: A systematic review. Front Endocrinol. 2023;14:1126637.