# Incidental Thyroid Nodules on the COVID-19 Positive CT Chest

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## ABSTRACT
**Background:** The recent widespread of COVID-19 led to a marked increase in the number of CT chest examinations. This led to frequent encounters of associated incidental findings as thyroid nodules. Thyroid imaging reporting and data system (TI-RADS) using variable ultrasound feature-allowed systematic reproducible approach for diagnosis and management of thyroid nodules.
**Objective:** This study aimed to detect the prevalence of incidental thyroid nodules in CT chest for COVID-19 cases as well as the percentage of malignant nodules among them and the concordance of TI-RADS classification with fine-needle aspiration cytology (FNAC) results.
**Patients and methods:** This retrospective study included 895 patients with CT findings of COVID-19 pneumonia. 203 patients were excluded due to absent PCR confirmation of COVID-19, lack of ultrasound confirmation of thyroid nodules or lack of FNAC results, so our study included 692 patients with confirmed COVID-19 pneumonia.
**Results:** A solitary thyroid nodule was discovered in 134 CT chest scans of 692 patients with confirmed COVID-19 pulmonary pneumonia, with a 19.4% incidence. These patients underwent ultrasound evaluation for the thyroid nodule. The nodules with TI-RADS 1-3 score were considered benign yet those with 4-5 score were classified as malignant. The results of the FNAC were compared to the thyroid TI-RADS classification, with nodules classified as Bethesda II-III being benign and those classified as Bethesda IV to VI being malignant.
**Conclusion:** Incidental thyroid nodule discovered during CT chest examination is an important finding and should be investigated and categorized using the TI-RADS system as even though the incidence of malignancy is not high, early diagnosis of thyroid malignancy can have a huge effect on the patient outcome.
**Keywords:** COVID-19, thyroid nodule, CT, US, TI-RADS.

## INTRODUCTION

The coronavirus disease 2019 (COVID-19) is a rapidly spreading infection across the globe with 5-15 % of the affected patients developing severe respiratory illness [(1-4)].

CT chest is a safe and rapid examination for diagnosing patients with suspected infection as it allows assessment of the degree of lung affection especially with the development of CT severity score, which allow assessment of the extent of lung involvement [(5-8)].

The huge number of patients performing computed tomography (CT) chest examination had led to the frequent encountering of incidental findings, one of which is incidental thyroid nodules. Incidental thyroid nodule is considered common findings in the cross-sectional imaging of the neck constituting about 16 to 18 % [(9-10)].

The American thyroid association stated that all incidental thyroid nodules should undergo further workup by ultrasound as there are no definite features in CT that can differentiate benign from malignant lesions [(11-12)].

The thyroid imaging and reporting data system (TI-RADS) is based upon specific ultrasound (US) features including size, shape, composition, margins, echogenicity and calcification. It aims to standardize the classification of thyroid nodules and limit fine needle aspiration cytology (FNAC) [(13)].

However, this created another debate about whether further investigation for incidental findings is of clinical value or is it a waste of resources on further investigation of findings that are mostly benign and unrelated to the patient complaint [(14-16)].

The aim of our study was to detect the prevalence of incidental thyroid nodules in patients performing CT chest for assessment of COVID-19 pneumonia and the percentage of malignant thyroid nodules discovered by further investigation of this incidental finding.

## PATIENTS AND METHODS

Between September 2020 and November 2021, 895 patients with CT findings of intermediate to a high probability of COVID-19 pneumonia (CO-RADS 3, 4 and 5) were included in this retrospective study. A negative RT-PCR confirmation resulted in the exclusion of 73 patients.

69 patients were excluded because the ultrasound (US) confirmation of the thyroid nodule was missed (36 patients with known nodular thyroid disease and 33 patients who couldn’t be assessed by the US). 61 patients were also excluded because the FNAC result was unavailable, so our study included 692 patients with confirmed COVID-19 pneumonia **(Figure 1)**.



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**Ethical approval:**

**The study was approved by The Regulatory Board of the hospital which waived the need for written consent. All procedures performed were under the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008.**

**Technique of the CT chest examination:**

Non-contrast high-resolution chest CT examination was done using eight MDCT (Siemens Healthineers, Erlangen, Germany). The patient was positioned supine with both arms raised .The scan was caudocranial and a scout was taken starting from 1 cm below the lowest costo-phrenic angle to 1 cm above the lung apices. The thickness of the non-contrast CT chest was 1.25 mm, the interval was 0.625 mm, the matrix was 512 X 512, the KV was 120, the mA was 150-400, and the rotation time was 0.5 seconds. All CT images were viewed on a dedicated workstation, and they were reconstructed using multi-planar reformation and viewed in different planes.

**Technique of the US examination:**

A 9L (2-8 MHz) linear-array probe was used to perform the ultrasound of the thyroid gland using LOGIQ S8, GE Healthcare (USA). Each nodule was scanned longitudinally and transversely, with an additional scan based on the characteristics of the nodule.

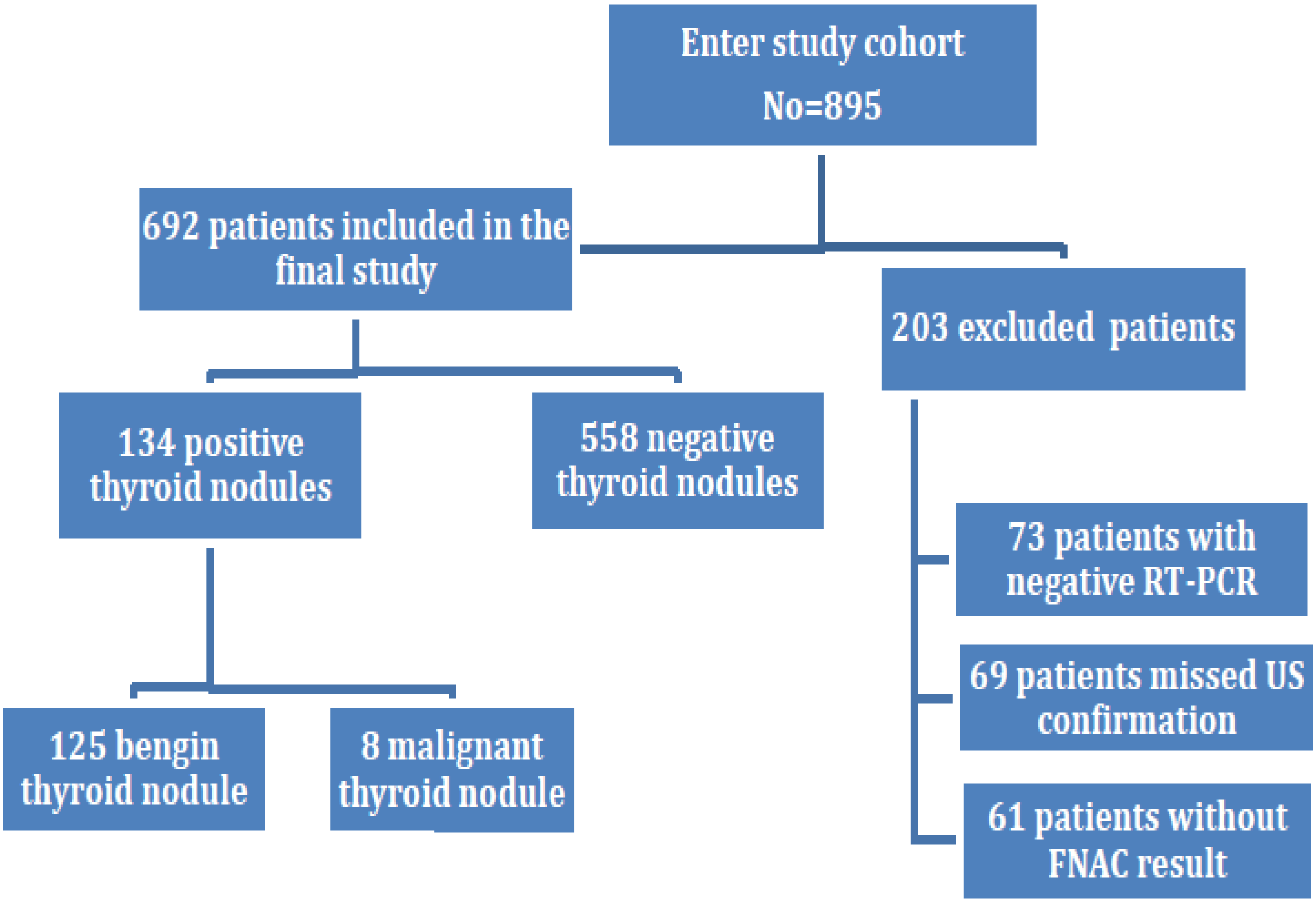


**Figure (1):** Flow chart of research methodology and results.

**Imaging Evaluation:**

All CT images were reported by a radiologist with 8 years of experience in chest imaging. COVID-19 pneumonia was diagnosed according to the COVID-19 Reporting and Data System (CO-RADS) classification: CO-RADS 1 (possibility of COVID-19 is unlikely): CT shows either normal appearance or findings of other non-infectious diseases, CO-RADS 2 (possibility of COVID-19 is low): CT shows imaging findings matching with other infections rather than COVID-19, CO-RADS 3 (uncertain whether COVID-19 is present or not): CT shows imaging findings matching with the presence of infection, CO-RADS 4 (high level of suspicion for COVID-19): CT shows imaging findings matching with a COVID-19, however not extremely typical such as unilateral ground glass patches, or multifocal pulmonary consolidations, CO-RADS 5 (very high level of suspicion for COVID-19): typical CT findings in the CT shows matches with COVID-19 [17].

All thyroid US images were reviewed by a radiologist with 6 years' experience in thyroid US who reported the composition, echogenicity, shape, margin, and calcification/echogenic foci using the American College of Radiology (ACR) TI-RADS sonographic category feature, then each category had assigned points. Finally, the points of each category were added together and the ACR TI-RADS (TR) score was assigned as follow; 0 point (TR1), 2 points (TR2), 3 points (TR3), 4 to 6 points (TR4), and 7 points or more (TR5) [18]. The nodules with TI-RADS 1-3 score was considered benign yet those with 4-5 score was classified as malignant. The results of the FNAC were compared to the thyroid TI-RADS classification, with nodules classified as Bethesda II-III being benign and those classified as Bethesda IV to VI being malignant.

**Statistical analysis:**

The Statistical Package for Social Science was used to analyse the data (IBM SPSS statistics for windows, V. 22.0, Armonk, NY, USA). The mean and range of quantitative data, as well as the number and percentage of categorical data, were expressed. Cross-tabulation was used to assess the diagnostic performance of the categorical variable, and the sensitivity, specificity, and accuracy were calculated.

**Results:**

One hundred thirty-four patients (134/692) with confirmed COVID-19 pneumonia and an accidental discovery of thyroid nodules, which was confirmed by US examination were included in our study. They involved 86 females (64.2%) and 48 males (35.8%) with a mean age of 36 ± 5.9 years (age range: 26 to 53 years). The imaging features of COVID-19-associated pneumonia in patients with thyroid nodules were affecting both lung parenchyma in 113/134 (84.3%) patients, while unilateral lung affection was seen in 21 (15.7%) patients. As regards disease pattern, multiple predominantly peripheral ground-glass opacity patches (GGO) were seen in 109 (81.4%) patients, while 20 (14.9%) patients had both pulmonary consolidation and ground glass patches, and the interlobular septal thickening with crazy-paving appearance was seen in only five (3.7%) patients (Table 1). According to the CT severity score [19], 118 (88.1%) patients had mild pulmonary involvement, 13 (9.7%) patients had moderate pulmonary involvement, and three (2.2%) patients had severe pulmonary involvement.

**Table (1):** Demographic and imaging data of the study population

| Characteristics | Number |
|---|---|
| **Age (mean ± SD)** | 36 ± 5.9 years |
| **Gender** | |
| Females | 86 (64.2%) |
| Males | 48 (35.8%) |
| **Imaging features** | |
| Bilateral | 113 (84.3%) |
| Unilateral | 21 (15.7%) |
| **Pneumonic pattern** | |
| Ground glass patches | 109 (81.4%) |
| Ground glass and consolidation patches | 20 (14.9%) |
| Interlobar septal thickening | 5 (3.7%) |

Thyroid nodules were observed in 134 CT chest scans of 692 patients with confirmed COVID-19 pulmonary pneumonia, with a 19.4% incidence. According to the FNAC, nine malignant thyroid nodules (Bethesda IV to VI) were discovered, with a 1.3% (9/692) incidence, while 125 benign thyroid nodules were discovered (Bethesda II-III). The malignant thyroid nodules were histopathologically diagnosed as five papillary thyroid carcinomas, three follicular carcinomas, and one follicular variant of papillary thyroid carcinoma (Table 2).

**Table (2):** Incidence of all thyroid nodules and the malignant thyroid nodules

| Thyroid nodules | Number | Incidence |
|---|---|---|
| Solitary thyroid nodule | 134/692 | 19.4% |
| Malignant thyroid nodule | 9/692 | 1.3% |

Table (3) revealed that seven thyroid nodules had a TI-RADS 4 score, four of which were malignant and three of which were benign, whereas four of five TI-RADS 5 score nodules were malignant and one was benign. Thyroid nodules with TI-RADS 1, 2, and 3 scores were found in 20, 15, and 87 thyroid nodules respectively, with 121/122 thyroid nodules classified as benign **(Figures 2 & 3)**. The sensitivity, specificity and accuracy of TI-RADS for diagnosing malignant thyroid nodules were 88.9%, 96.8% and 96.3% respectively.

**Table (3):** Number of thyroid nodules according to the ACR TI-RADS classification and the FNAC result

| TI-RADS score | Bengin FNAC | Malignant FNAC | Total |
|---|---|---|---|
| TI-RADS 1 | 20 (16%) | 0 | 20 (14.9%) |
| TI-RADS 2 | 15 (12%) | 0 | 15 (11.2%) |
| TI-RADS 3 | 86 (68.8%) | 1 (11.2%) | 87 (64.9%) |
| TI-RADS 4 | 3 (2.4%) | 4 (44.4%) | 7(5.3%) |
| TI-RADS 5 | 1 (0.8%) | 4 (44.4%) | 5(3.7%) |
| Total | 125 | 9 | 134 |

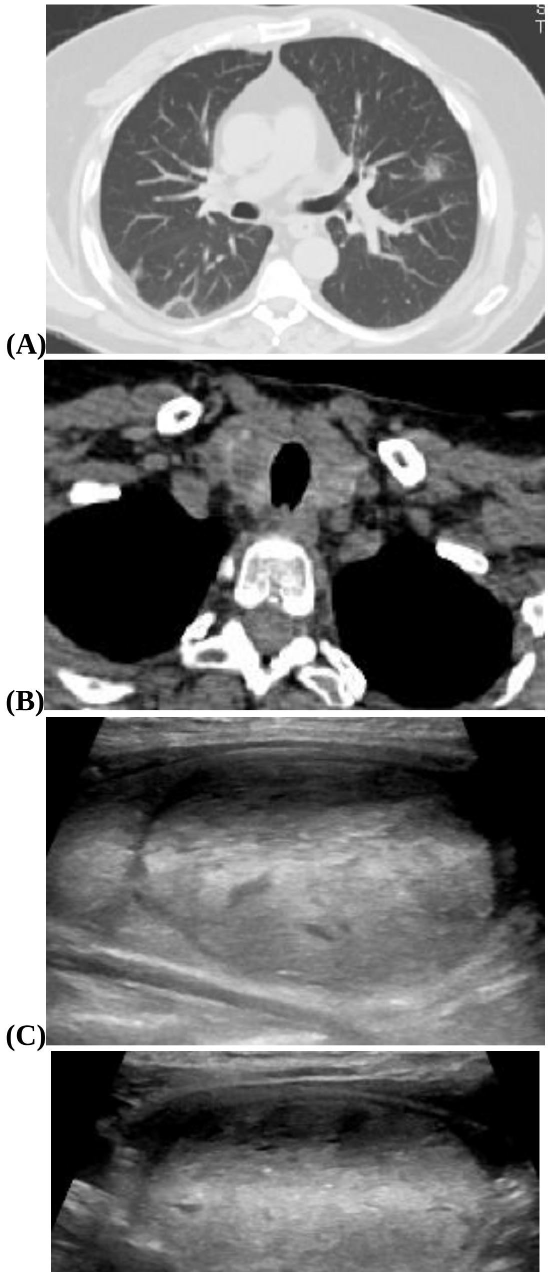

**Figure (2):** 30-year-old female with COVID-19 (A) CT chest shows bilateral peripheral ground-glass opacity (CORADS 5) with an accidental discovery of right thyroid lobe nodule (B). US (C) and (D) revealed well defined wider than tall isoechoic solid nodules (TI-RADS 3), FNAC revealed Bethesda II.

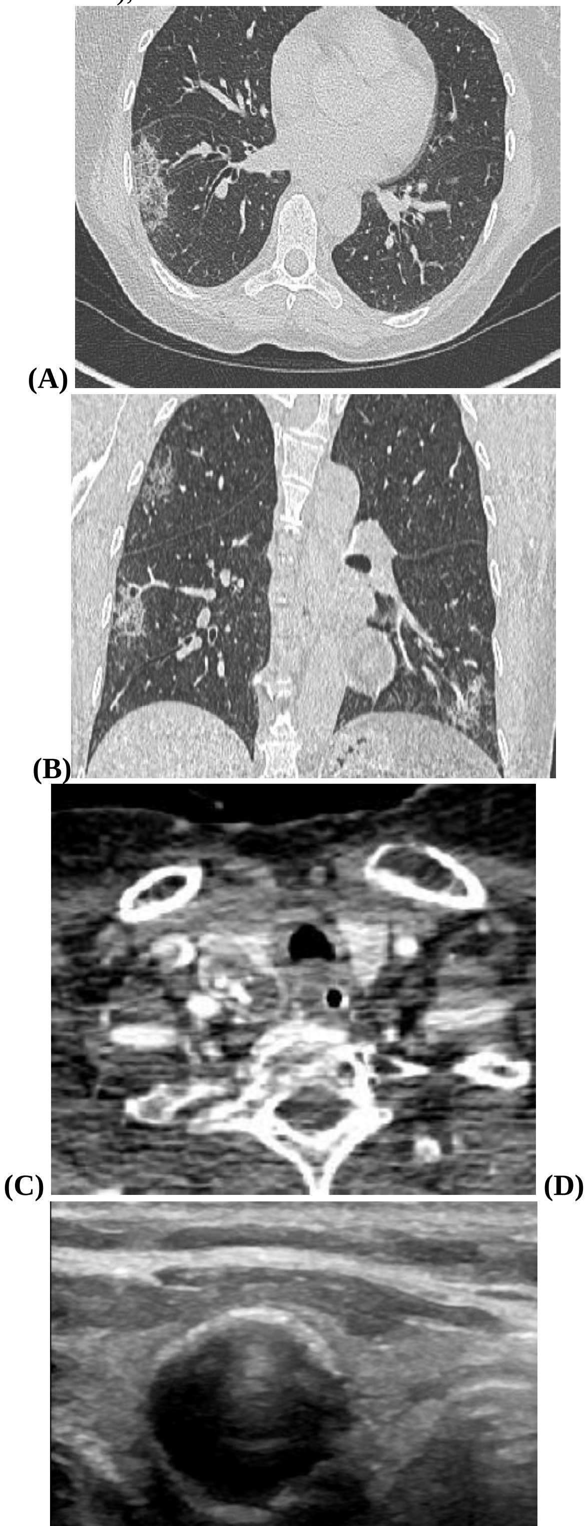

**Figure (3):** 35-year-old male patients with COVID-19 (A),(B) and (C)CT chest shows bilateral peripheral ground-glass opacity with an accidental discovery of right thyroid lobe nodule (D) US revealed well defined taller than wide solid nodule with indeterminate content (TI-RADS 5), FNAC revealed Bethesda V.

## DISCUSSION

CT chest is a rapid and efficient diagnostic tool for COVID-19 patients as it accurately determines the extent of lung affection. There is a wide range of lung manifestations that can be seen in the CT chest of COVID-19 patients yet predominant ground-glass opacities in lung regions close to pleural surfaces, with or without consolidations, and a multifocal bilateral distribution are considered highly suspicious for COVID-19 pneumonia (CO-RADS 4 and 5) [20].

However, the focus of our study was not the lung findings but the associated incidental findings of thyroid nodules at the scanned lower neck cuts especially with the spread of COVID-19 cases and subsequent increase in the CT chest examination, which led to the frequent detection of such incidental finding. So the current study is relatively unique as it focused upon incidental thyroid nodules only unlike the study done by **Munden *et al.*** [21] that discussed the management of incidental cardiovascular and mediastinal findings in general.

The current study revealed that the incidental thyroid nodules were found in 19% of COVID-19 patients, with thyroid cancer accounting for about 1.3%, which was comparable to the global prevalence of incidental thyroid nodules, which ranges from 19 to 67%, with thyroid cancer accounting for 5 to 15% of these nodules [22-23]. Although those patients had more extensive and serious lung affection, further investigation by ultrasound is clearly stated within the American thyroid association guidelines to exclude malignancy even though the incidental thyroid nodules are usually benign [11-12].

TI-RADS classification allowed a standardized form for stratification of thyroid nodules into those requiring FNAC and those of benign nature with no need for such intervention thus reducing the costs and side effects for investigating thyroid nodules and allowing easier standardized communication between the radiologist and clinicians, which in turn made the examination and stratification of patients with thyroid nodules relatively a straightforward task [13].

Many TI-RADS classifications have been released, each with a minor difference in their criteria and subsequent patient management; the most well-known are those released by the American College of Radiology (ACR TI-RADS), European thyroid association (EU-TI-RADS), and Korean society of thyroid radiology (K-TI-RADS) [24-26]. The current study relied on the ACR-TI-RADS because it has the highest sensitivity and negative predictive values with relatively high specificity and positive predictive value [27] which was critical as the primary goal of this study was thyroid cancer diagnosis since early diagnosis and management has a massive impact on patient outcome.

The degree of concordance between TI-RADS and FNAC results is of utmost importance as the effectiveness of the TI-RADS system depends upon the extent of such concordance. **Tanpitukpongse *et al.*** [28] discovered an incidental thyroid nodule in 37% of cases, with malignancy detected in 6%, which is relatively higher than our study, which revealed 19.4% incidence of thyroid nodule with 1.3% malignancy since our study included only patients undergoing CT chest due to suspected COVID-19 infection, whereas **Tanpitukpongse *et al.*** [28] involved all cross-section CT and MR studies performed for many different reasons. In a study done by **Periakaruppan *et al.*** [29]**,** the proportion of malignant thyroid nodules that were assigned by ultrasound as TI-RADS 2, 3, 4, and 5 were 0%, 7.7 %, 38.4 %, and 53.9 %, respectively, which is similar to our study which was 0%, 11.2 %, 44.4 %, and 44.4 % respectively. However, a different percentage was observed in a study conducted by **Schenke *et al.*** [24] where the proportion of malignant thyroid nodules assigned TI-RADS 2, 3, 4, and 5 were 0%, 0%, 30.3 %, and 69.7 %, respectively, which can be explained by the fact that they only considered small nodules less than 10 mm.

The main limitation of our study was that we did not correlate the TI-RADS and the FNAC results with specific findings at CT as size or associated lymphadenopathy as the CT chest did not show the entire thyroid or the neck, which prevented proper measurement of the size as well as assessment of associated lymphadenopathy.

## CONCLUSION

Even though the incidence of thyroid cancer is low, an incidental thyroid nodule discovered during a CT chest examination is a significant finding that should be investigated and classified using the TI-RADS system, because early diagnosis of thyroid cancer has a s

ignificant impact on the patient's final outcome.

**Abbreviation:** Coronavirus disease of 2019: COVID-19; Computed tomography: CT; Thyroid Imaging Reporting and Data System: TI-RADS; Ultrasound: US; Fine needle aspiration cytology: FNAC; COVID-19 Reporting and Data System: CO-RADS; Ground-glass opacity patches (GGO); American College of Radiology: ACR; European thyroid association Thyroid Imaging Reporting and Data System: EU-TI-RADS; Korean society of thyroid radiology: K-TI-RADS.

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