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Pulmonary Thromboembolism on CT Pulmonary Angiography of Covid-19 Patients and Its Correlation to CT Severity Score, D-dimer, and Ferritin Levels: A Prospective and Retrospective Study

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Abstract

Background: PTE risk has been linked to SARS-CoV-2. The purpose of this study was to identify the clinical manifestation and contributing causes of death in COVID-19-infected hospitalized patients.

Method: The prospective and retrospective data included patients who tested positive for RT-PCR irrespective of age and gender. Sample size is 291. Statistical Significance is done using Parametric tests such as t-test categorical variables tested by chi-square test.

Results: A total of 291 subjects were involved in this study. Of the total population, 76.3% of the participants had positive COVID-19 status, while 23.7% of the participants were post-COVID-19. 24.1% of the participants had very mild CT-SS, 0.3% had mild CT-SS, and 26.5% had moderate CT-SS: Moderate. Only 0.3% of the participants had severe CT-SS, while 48.8% had very severe CT-SS. patients having very mild disease have less clinical suspicion of having PTE. PTE among patients was positively associated with higher D-dimer levels (4048.75 ± 2946.93 ng/mL to 1875.25 ± 2135.72 ng/ml, respectively). Patients who tested positive for PTE had higher ferritin levels than those without PTE (487.79 ± 690.42 ng/ml to 409.50 ± 409.09 ng/ml, respectively).

Conclusion: Higher the severity(inflammation) higher the risk of formation of thrombus. Patients with higher CT severity score and D-dimer levels and with clinical suspicion of PTE should undergo CTPA.If patient cannot undergo CTPA when there is a suspicion of PTE in severe and very severe covid disease it is safe to start therapeutic thromboprophylaxis.

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Abbreviations

SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; MERS: Middle east respiratory syndrome; RT-PCR: Reverse transcription polymerase chain reaction; RNA: Ribonucleic acid; ADE: Antibody-dependent enhancement; ARDS: Acute respiratory distress syndrome; RAS: Renin angiotensin system; ACE-2: Angiotensin-converting enzyme-2; DIC: Disseminated intravascular coagulation; PTE: Pulmonary thromboembolism; PT and PE: Prothrombin time and pulmonary embolism; APTT: Activated partial thromboplastin time; CRP: C-reactive protein; IL-6: Interleukin 6; LDH: Lactate dehydrogenase; CT:Computed tomography; CTPA:Computed tomography pulmonary angiogram; DVT: Deep vein thrombosis; ICU: Intensive care unit; CT-SS: Computed tomography severity score; MPA: Main pulmonary artery; RUL: Right upper lobe; RML: Right middle lobe; RLL: Right lower lobe; LUL: Left upper lobe; LLL: Left lower lobe; WHO: World health organization.

Introduction

Coronavirus disease (COVID-19) is now considered a significant threat to public health caused by SARS CoV-2. WHO announced the COVID-19 outbreak as a global pandemic on 11 March 2020. RT-PCR is a well-established and recommended diagnostic test that detects viral RNA.

Burden of disease

According to the WHO, the following (Table 1) were the COVID-19 statistics crisis globally and in India as of 18 September 2020 [1].

Table 1: COVID-19 statistics as on 18 September 2020 [1].

	India	World
Total confirmed cases	5,214,677	30 million+
Total deaths	84,372	946,430

The primary infection initiates alveolar injury and the resulting inflammatory response, including the production of inflammatory cytokines, including IL-6 [2]. Similarly, it contributes to the activation and recruitment of mononuclear cells and neutrophils, causing more tissue damage, including damage to the capillary endothelium. Thrombo-protective state of the vascular endothelial cells is disrupted. In thromboinflammation, endothelial cells lose the normal antithrombotic and anti-inflammatory functions, leading to dysregulation of coagulation, complement, platelet activation, and leukocyte recruitment in the microvasculature.

Patients with severe COVID-19 often have abnormal laboratory markers in systemic inflammatory reactions. The biomarkers that have a prognostic value include CRP, D-DIMER, Serum LDH, serum ferritin, and IL- 6.

Role of CT in COVID-19

High-resolution CT is considered a standard method for diagnosis of COVID-19 (Table 2). It has low rate of missed diagnosis (3.9%) but is not recommended as standard diagnostic method due to very low specificity(37%). A systematic review of 13 studies revealed a positivity rate of 90% for CT imaging [3].

Table 2: Risk stratification of COVID-19 suspected patients based on CT findings.

Co-rads	Level of suspicion	Summary
0	not interpretable	scan insufficient for assigning a score
1	very low	normal or non-infectious
2	low	typical for other infections but not covid
3	equivocal/indeterminate	features compatible with covid but also other diseases
4	high	suspicious
5	very high	typical
6	proven	RT-PCR positive

Typical signs

Ground glass opacities with consolidation, Pleural thickening, Interlobular septal thickening, and Air bronchograms [4].

Atypical signs

Crazy paving pattern, Lymphadenopathy, Bronchiectasis, Pleural effusion, Fibrosis, and Nodules [4].

CTPA in detecting thromboembolism

Diagnostic criteria: (1) Complete occlusion or enlargement of a vessel compared with the adjacent patent vessel, (2) Partial filling defect (mint polo sign and railway track sign), (3) Eccentric emboli (making an acute angle with the wall), (4) Ancillary findings – Wedge-shaped hyper attenuation in the lung, the linear band in the lung, short axis of right ventricle greater than the left ventricle, hyper attenuation of thrombus itself in the plain scan, contrast reflux into inferior vena cava and hepatic veins, deviation of interventricular septum towards the left ventricle (Figure 1 and Figure 2).

Role of D-dimer levels in COVID-19 related to PTE

D-dimer is the degradation product of crosslinked fibrin. The reference concentration of D-dimer is < 250 ng/ml, or < 0.4 mcg/ml. A normal D-dimer level provides reasonable confidence that PE/DVT is not present, but we cannot safely exclude PE in a patient with high pre-test probability.

Role of ferritin levels in COVID-19

Hyperferritinemia (ferritin level > 400 μg/L) observed in patients

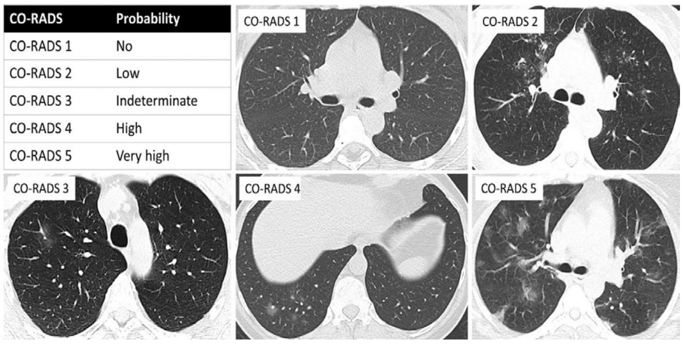

Figure 1: Axial CT plain images showing CORADS grading.

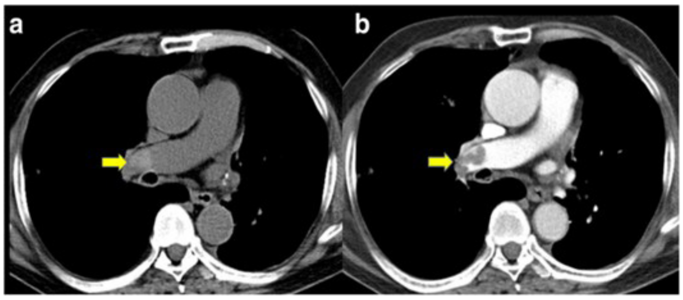

Figure 2: CT images of a patient with dyspnoea and diagnosed with PTE. **(a)** non-contrasted CT illustrating high attenuation emboli in the right pulmonary artery (arrowhead). **(b)** post-contrast illustrating filling defects in the right pulmonary artery.

with severe disease. Hyperferritinemia is key acute-phase reactant [4]. Ferritin apart from classic role as an iron storage protein, also functions as a signalling molecule and direct mediator of the immune system [5].

Review of Literature

Pulmonary thromboembolism in COVID-19 patients. PE has been frequently reported among COVID-19 patients and is primarily noted in patients without other risk aspects, signifying that it is an independent risk for venous thromboembolism [6]. Endothelial cell activation is the main driver for the intensifying and realized thrombosis complications. According to Varga et al., viral inclusion bodies have been realized in endothelial cells in different organs, ranging from the lungs to the gastrointestinal tract [7]. The rapid and viral replications lead to the enormous release of inflammatory mediators.

Bompard et al.'s retrospective study on 137 patients highlights that high D-dimer level is associated with high thrombotic incidences among patients admitted to the ICU [8]. Additionally, Whyte et al.'s [9] retrospective review note that COVID-19 influences systemic inflammation and increases the risk for DVT, with PE observed in approximately 16.70% to 47.0% of patients admitted to ICU [10].

Kaminetzky et al.'s [11] retrospective study evaluates PE prevalence at CTPA in 62 COVID-19 patients and aspects associated with its severity. According to the authors, more than 37.0% with COVID-19 underwent CTPA evaluations diagnosing PE. The results indicate that PE can lead to decompensation among COVID-19 patients. Liao et al.'s systematic review and meta-analysis annotates that severe COVID-19 complications related to coagulation has increased fibrinogen and D-dimer level with high risks of thrombus [12].

Acar et al.'s health analysis study reveals that the occurrence of DVT and PE is more significant among patients with COVID-19 history or suffering from the pandemic [13]. Gómez et al.'s systematic review and meta-analysis points out that thrombotic complication risks among COVID-19 patients are higher, between 20% and 25%, compared to the general population with only an 8% lifetime risk [14]. Fauvel et al.'s cohort study backs Gómez et al.'s study by highlight that the male gender is a risk factor for PE in COVID-19 patients [15].

Velavan et al.'s study highlights that D-dimer reflects the unending activation of the haemostatic structure and obliges as a thrombosis indicator [16]. Consequently, there is a significant association between the circulating D-dimer concentration and PE. Therefore, it is an accurate biomarker for mortality prediction among COVID-19 patients. It has better sensitivity and specificity; hence, it can be an easy-to-perform and cheaper laboratory indicator for the prognosis of COVID-19.

CT score in assessing COVID-19

Nokiani et al.'s retrospective study annotates that comorbidities that aggravate COVID-19 severity results in immune system disturbance and more widespread inflammation leading to higher CT-SS [17]. Therefore, CT-SS is an illness quantifying equipment in COVID-19 (Table 3). Aziz-Ahari et al.'s cross-sectional study mentions that CT imaging in predicting disease severity during its early stages is significant and valuable for efficiently handling the disease spread [19].

Table 3: CT-SS in COVID-19.

Severity grade	Total score in percentage
Very mild	LESS THAN 5% (< 1.25)
Mild	6 - 25% (1.25 to < 6.25)
Moderate	26 - 50% (6.25 to < 12.5)
Severe	51 - 75% (12.5 to < 18.75)
Very severe	GREATER THAN 75% (> 18.75)

D-dimer level in relation to COVID-19 severity and PE incidences

Severe acute respiratory syndrome infections resulting from COVID-19 are associated with intensified inflammatory levels and prothrombotic biomarkers such as elevated D-dimer levels and IL-6 [20]. The retrospective study by Lopez-Castaneda et al. shows that the median D-dimer level was lower in the general population (1269 ng/ml) and significantly higher in PE-positive patients than negative PE patients (4013 ng/ml to 1198 ng/ml, respectively).

Léonard-Lorant et al.'s prospective study reports that patients who tested positive for COVID-19 infection and had PE had elevated levels of D-dimer than patients without PE. Furthermore, two Indian studies have explained the role of D-dimer levels in COVID-19 infection and its elevation risks in making the outcomes adverse [20, 21]. Mishra et al. [21] explain that comorbidities existence example(diabetes) among severe positive COVID-19 patients is associated with adverse prognosis. Secondly, Rathi et al.'s [20] study annotates that PTE is common in high-altitude locations [20]. The authors explain that in high altitudes, there is an elevated positive predictive value of D-dimer among individuals, contributing to common incidences of PTE [20].

Serum ferritin level in relation to PE positivity and COVID-19

According to the Pan American Health Organization and the WHO, ferritin is a critical mediator for immune dysregulation [22]. It functions as a mediator remarkably under hyperferritinemia through direct pro-inflammatory and immune-suppressive impacts leading to the cytokine storm [22]. Gómez-Pastora et al. review indicate that the concentrations of serum ferritin were within the normal range among patients with non-severe diseases such as COVID-19 infection. The study also reports that COVID-19 patients who were admitted to hospitals and did not survive showed higher serum ferritin levels. Marwah et al.'s [23] retrospective analysis and Carubbi et al.'s [24] prospective study points out that serum ferritin has been suitably characterized as a severe phase reactant and a linkage of immune dysregulation in severe COVID-19.

Research Question, Aims, and Objectives

Research question

Can CT severity score help to predict the risk of pulmonary thromboembolism in COVID-19 disease?

Aim of the study

The aim of the study is to see the association between CT chest severity grade and presence of pulmonary thromboembolism in CTPA and correlate it with D-dimer, and ferritin levels in COVID-19 patients.

Objectives of the study

1. To calculate the prevalence of PTE in COVID-19 patients with suspected pulmonary thromboembolism.

2. To evaluate the association between patients with pulmonary thromboembolism and CT severity scores at the time of conducting CTPA.

3. To Correlate D-Dimer and ferritin levels of covid patients with positive pulmonary thromboembolism on CTPA.

Materials and Method

Study design

This prospective and retrospective study was based on the Department of Radiology.

Study population

The prospective and retrospective data included patients who tested positive for RT-PCR irrespective of age and gender. Similarly, the study included patients with clinically suspected PE.

The inclusion criteria were as follows:

- Patients with covid RT-PCR positive and clinically suspected pulmonary thromboembolism.
- Patients in whom D-Dimer and ferritin correlation is available.

Patients were excluded if they had the following:

- Patients allergic to iodinated contrast media.
- Patients in whom contrast media are contraindicated.
- Patients who are known cases of pulmonary thromboembolism.
- Patients who did not consent to be a part of the study.

Data collection: imaging procedure

COVID-19 patients with suspected PE were taken for the study according to the institution protocol using a 16-slice CT scanner (PHILIPS), and a 1 mm contiguous slice was taken. Both pre- and post-contrast scans were performed. Non-ionic water-soluble iodinated contrast medium (Omnipaque 350) was administered as a bolus dose at a rate of about 4 ml/sec with 18 gauze needles. The dose was titrated according to the weight of the patient. Immediately after the completion of the bolus injection, a CT scan of the chest was obtained.

Sample size

Both prospectively and retrospectively, all the patients meeting the inclusion criteria during the study period were enrolled.

N = z2PQ/L2

N = sample size

Z = 1.96 at 95% CI

P (prevalence) = 23 - 25% (PTE varying among COVID 19 patients 23 - 25%) by Bompard et al. [8].

Q = 100 – 23 = 77%

L = 5% (Precision)

N = 3.84 x 23 x 77/5 x 5

N = 272.02

Making it to near value sample size considered is 280.

Statistical analysis

Data entry was done using M.S. Excel and statistically analysed using Statistical package for social sciences (SPSS Version 16) for MS Windows. Descriptive statistical analysis was conducted to explore the distribution of several categorical and quantitative variables. Categorical variables were summarized with percentages (%), while mean ± SD summarized quantitative variables. All results were also presented in tabular form and are shown graphically using a bar diagram or pie diagram as appropriate. Inferential Statistics: The difference in the two groups were tested for Statistical Significance using Parametric tests such as t-test categorical variables tested by chi-square test. A p-value less than 0.05 is considered statistically significant.

Ethical Approval

This project was approved by the hospital ethics committee.

Results

Patient characteristics and data

Based on the selection criteria, a total of 291 subjects were involved in this study (217 males and 74 females). The participants' mean age (years) was 55.68 ± 13.70 (standard deviation). Of the total population, 76.3% of the participants had positive COVID-19 status, while 23.7% of the participants were post-COVID-19. 24.1% of the participants had very mild CT-SS, 0.3% had mild CT-SS, and 26.5% had moderate CT-SS: Moderate. Only 0.3% of the participants had severe CT-SS, while 48.8% had very severe CT-SS. Additionally, only 3.4% of the participants had additional comorbidities.

COVID-19 status among patients

In our patients (n = 291), 222 patients (76%) have active COVID-19 disease and 69 patients (23.7%) are post covid patients. It's been observed that positive COVID-19 patients had higher CT-SS (6.25 - 12.25) than post-COVID-19 patients. Very severe CT-SS was highly recorded in positive COVID-19 patients than post-COVID-19. The number of post-COVID-19 patients were the lower than positive COVID-19 patients.

CT severity in our subjects

It has been noted that 'very severe' group (score: > 18.75) recorded highest number (n = 90) and very mild group recorded the lowest (n = 17). Indicating that patients having very mild disease have less clinical suspicion of having PTE.

Very severe cases of CT severity were the highest in percentage while very mild cases were the lowest among the patients. Most participants showed very severe CT severity (31%), followed by moderate cases (26%) while the lowest cases displayed very mild CT severity (6%).

CT Severity correlation with D-dimer (ng/ml), ferritin (ng/ml), MPA diameter (mm), and PTE Location (especially in the RUL Lobar, RUL- Apical, RLL- Lobar, LUL- Upper Division, and LUL- Lower Division).

PTE on CTPA and its association with CT severity score

In our study it has been recorded that 17.9% (n = 52) of the participants show PTE on CT. Remarkably, only 5.8% of the PTE on CT group participants had additional comorbidities. Only 17.9% of the patients tested positive of PTE after CT scan while 82.1% showed absence of PTE on CT.

PTE was more located in the right lower lobe posterior segment (71.2%) and least located in the main pulmonary artery (2.0%). The presence of PTE was more frequent among patients with severity group 'moderate and higher 'than compared to patients with mild or very mild severity grade PTE (Figure 3).

D-dimer levels

PTE among patients was positively associated with higher D-dimer levels (4048.75 ± 2946.93 ng/ml to 1875.25 ± 2135.72 ng/ml, respectively). There was higher D-dimer level among positive CTPA COVID-19 patients (2340.14 ± 2539.59 ng/ml) compared to post-COVID-19 patients (2017.51 ± 2098.44 ng/ml). The analysis between D-dimer and age groups of participants produced a significant correlation (rho = 0.22, p = 0.009). Remarkably, for every increase in age among the participants per unit, there was an increase in the D-dimer level by 20.43 units. There was a significant difference among the seven age groups evaluated in D-dimer levels (χ^2 = 17.021, p = 0.009), with the median D-dimer being highest in the age group of 71 - 80 years. There was a positive correlation between ferritin and D-dimer (ng/ml), and this correlation was statistically significant (rho = 0.16, p = 0.007). Besides, there was a significant difference between the five groups in terms of D-dimer (χ2 = 12.813, p = 0.012), with the median D-dimer being highest in the CT-SS of between 12.25 - 18.75 group. Positive PTE patients on CT displayed higher D-dimer levels compared to patients with negative PTE on CT (Figure 4).

Serum ferritin levels

The median ferritin was higher in the male group than in the female group. D-dimer levels, CT-SS, CT Severity, COVID-19 Status, and PTE availability positively correlated with ferritin levels among participants ($p < 0.05$). Positive COVID-19 status among patients showed higher ferritin levels than post-COVID-19 patients (446.31 ± 499.11 ng/ml to 350.07 ± 360.99 ng/ml, respectively). Patients who tested positive for PTE had higher ferritin levels than those without PTE (487.79 ± 690.42 ng/ml to 409.50 ± 409.09 ng/ml, respectively). Besides, there was no statistical significance in age group variation about ferritin levels among the patients (χ^2 = 8.152, p = 0.227) (Figure 5).

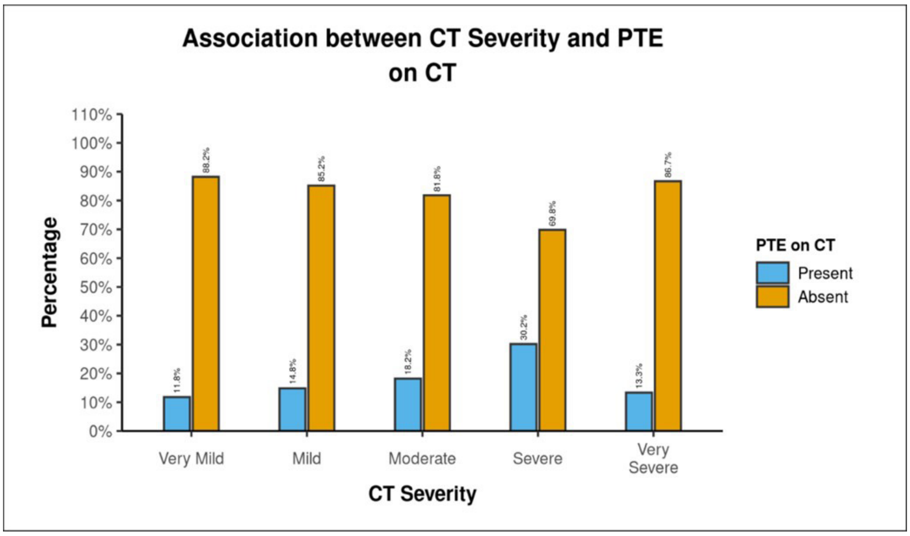

Figure 3: Association between CT severity and PTE on CT.

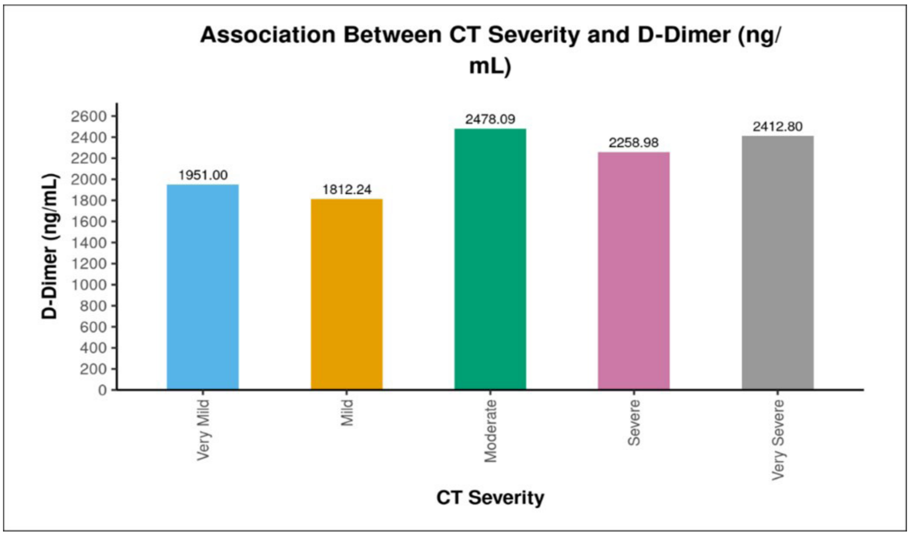

Figure 4: Association between CT severity and D-dimer (ng/ml).

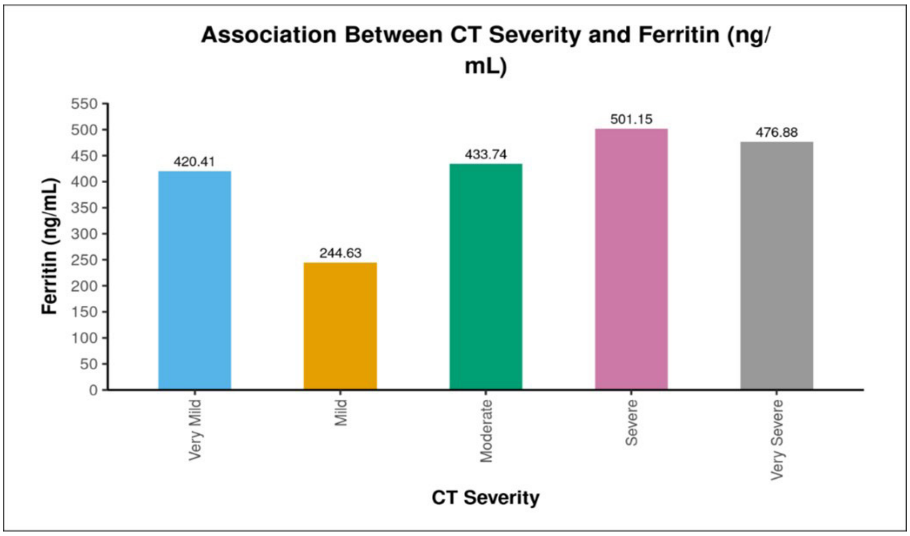

Figure 5: Association between CT severity and ferritin (ng/ml).

Discussion

In this study of patients with COVID-19 and post-COVID-19 who undertook CTPA, 17.9% of the subjects were positive for PTE. Out of this population, more males were positive than females, whereby 30.8% were females, and 69.2% were males. The CT severity was more among patients with PTE in each CT-SS groups compared to patients without PTE. PTE was more located in the right lower lobe posterior segment (71.2%) and least located in the main pulmonary artery (2.0%). Additionally, D-dimer levels are positively correlated with the degree of CT-SS.

In assessing the ferritin levels among the participants, there is a correlation between gender difference and ferritin levels. Specifically, the median ferritin was highest among men compared to women. Similarly, D-dimer and ferritin levels positively correlated among the participants. Positive COVID-19 status was associated with higher ferritin levels, while post-COVID-19 patients had a slightly low ferritin level. Similarly, PTE positive patients recorded higher ferritin and D-dimer levels than patients who did not show PTE in their CTPA. D-dimer levels of the patients has been positively associated with CT-SS groups (increasing with increasing severity grade) allowing us to predict the risk of PTE, considering association between CT-SS and PTE presence.

The MPA diameter of our patients with PTE is significantly higher compared to patients with negative CTPA. Similarly, MPA diameter of post covid patients is higher than positive COVID-19 patients.

According to Schafer, patients have hypercoagulable states when they have clinical conditions or laboratory anomalies associated with intensified thrombosis risk (prethrombotic conditions [25]. Cui and co-authors state that COVID-19 infection contributes to sepsis and the release of inflammatory cytokines such as IL-8 and IL-6, similar to the severe acute respiratory syndrome.

PE in COVID-19 patients has been described after the pandemic became widespread globally, beginning with small-series and single case reports. The findings from this study support two recently published radiology research literature highlighting 23.0% [26] and 30% [27] of CTPA evaluations to be positive in COVID-19-positive groups. For the positive PTE cases, more percent of men were affected compared to women. Men have lower survival rates than their women counterparts.

Llitjos et al.'s clinical reports reinforce the correlation between PTE and COVID-19, with the high peripheral venous thrombosis rate occurring among ICU patients [28]. A study by Whyte et al. also emphasizes that COVID-19 influences systemic inflammation and increases the risk for DVT, with PE observed in approximately 16.70% to 47.0% of patients admitted to ICU [10]. The 17.9% of subjects with PTE in this study's positive COVID-19 and post-COVID-19 groups was higher than the approximate 16.70% to 47.0% rate reported in Whyte et al.'s [10] study. When evaluating patients who were CTPA positive, 82.7% were COVID-19 positive, and 17.3% were post-COVID-19. Even though the high percentage of CTPA evaluations supports such findings, the intensified PTE risk in COVID-19 patients.

Given the relationship between COVID-19 with hypercoagulable states, prophylactic anti-coagulation can reduce mortality [29]. The results show that D-dimer is associated with high thromboembolic incidences. The correlation between pulmonary artery obstruction, thromboembolic events (PTE), and D-dimer levels can be used to indicate PTE severity among COVID-19 patients. The results indicated that the elevation of D-dimer level positively correlated with PTE obstruction for the right and left pulmonary arteries. Another Indian study by Rathi et al. [20] states that PTE is highly common in high-altitude locations [20]. In high altitudes, individuals have an elevated positive predictive value of D-dimer, contributing to common incidences of PTE [20].

Besides Mishra et al. [21] and Rathi et al. [20] studies, the association between PTE and D-dimer is much supported by other existing studies [8]. According to Bompard et al., the D-dimer level elevates more among PE-positive CTPA patients illustrating that the level increase is a marker of pneumonia severity and is linked to higher PE risk [8]. Also, Kaminetzky et al. note that D-dimer level and elevation significantly correlated with the level of pulmonary artery obstruction as appraised by the Mastora grading approach [9].

Solberg and Glass note that a value of 500 ng/ml is primarily utilized as a D-dimer positivity threshold for the general population. Older positive COVID-19 patients with elevated D-dimer levels were at higher risk of testing positive for PTE than the young ones. There was a significant and recognizable difference among the seven age groups analysed in this study in D-dimer levels.

Furthermore, the results from this study indicate that ferritin is closely correlated with COVID-19 severity among patients. Positive COVID-19 patients investigated displayed higher ferritin levels compared to post-COVID-19 patients. A previous study by Alroomi et al. shows that patients with very severe and severe COVID-19 conditions exhibit increased serum ferritin level [30]. Higher serum ferritin level was recorded among very severe COVID-19 patients [30]. Alroomi et al. note that most of the positive COVID-19 patients within a group that recorded more than 1000 ng/ml of ferritin level had shortness of breath, asymptomatic infection, fever symptoms, or headache [30]. Maddimani et al. report that severe COVID-19 in India was a hyper-ferritinemic syndrome [31].

Specifically, in our patients who tested positive for PTE had higher ferritin levels (487.79 ± 690.42 ng/ml) than those who tested negative for PTE (409.50 ± 409.09 ng/ml). Galland et al. state that the prevalence of thrombotic events is related to the combination of hypoxia with an immune-triggered thrombo-inflammation is a cause coagulability and endothelial injuries [32]. Since hyperferritinemia is linked to inflammatory states in severe acute respiratory COVID-19 infection, ferritin might probably be a convenient aspect to predict the severity of the disease and the level of the cytokine storm [23].

Marwah et al. [23] and Carubbi et al. [24] state that serum ferritin is suitably characterized as a severe phase reactant and a linkage of immune dysregulation in severe COVID-19 infection. Composite feedback approaches between cytokines and serum ferritin in controlling anti-inflammatory and pro-inflammatory mediators can be termed cytokines-inducing ferritin expression. It has been suggested that COVID-19 with PTE cases might be included within the hyperferritinemic syndrome.

Additionally, the findings show that gender difference and the presence of ferritin are statistically correlated. Specifically, the median ferritin level was higher in the male group than in the female group, showing that ferritin correlates with gender. The results align with the findings from Gandini et al., which report that male patients have a higher inflammatory reaction, with greater serum ferritin levels than females [33]. Through their sex-disaggregated data, serum ferritin levels increasingly intensify with disease severity, but male patients necessitate intensive care more frequently than women [33]. Therefore, it can be speculated that higher serum ferritin status among men could have led to worsening COVID-19 outcomes among male patients. Besides, CT severity availability positively correlated with ferritin levels and PTE positivity among participants. According to Yang et al. [16], the inter-reader and performance concordance of CT-SS can be the identifier of COVID-19 severity. Such findings are backed by Nokiani et al. study highlighting that comorbidities that aggravate COVID-19 severity results in immune system disturbance and more widespread inflammation by increased ferritin levels leading to higher CT-SS [17]. Therefore, this study shows that CT imaging in predicting disease severity during its early stages is significant and valuable for efficiently handling the disease's spread.

Summary

This was a prospective and retrospective study that evaluated 291 patients. The study assessed PTE positivity rate (prevalence) at CTPA in COVID-19 patients (those who tested positive and post-COVID19) and its association with CT severity. The study evaluated the association between D-dimer and ferritin levels of COVID-19 patients with positive PTE on CTPA.

The study was undertaken at Krishna Institute of Medical Sciences to achieve the objectives and aim of this study. A two-year study period lasted between May 2020 and September 2022. From the findings, 17.9% of the participants were positive with PTE on CT. Of the 17.9%, 30.8% were females and 69.2% were males in this study of positive COVID-19 and post-COVID-19 patients. In this study, D-dimer levels (ng/ml) were significantly higher among positive-PTE patients compared to patients who tested negative of PTE on CT. Similarly, D-dimer levels correlated with pulmonary artery obstruction and its severity ($p < 0.05$). Patients with 'severe' and 'very severe' grade on CT-SS have high prevalence of PTE than other severity groups (Table 4). On the other hand, serum ferritin level is a significant immune dysregulation mediator and impacts the severity of COVID-19 infection.

Table 4: Chest CT- SS Grading Assessment [17].

Severity grade	Involvement severity	Total score in percentage
No severity	0	0%
Very Mild	1	1% - 5%
Mild	2	5% - 25%
Moderate	3	26% - 49%
Severe	4	50% - 75%
Very Severe	5	More than 75%

D-dimer level can be utilized to classify and point out risks among patients in terms of severity and suspicion of PTE. CT-SS and imaging in forecasting the severity of a disease such as COVID-19 and PTE during its early stages are significant and valuable for efficient handling of the disease.

Conclusion

In our study with COVID-19 patients (n = 291), patients with high CT-SS (score- moderate and higher) have substantially high risk of PTE compared to very mild and mild groups, supporting the concept of thromboinflammation. Higher the severity (inflammation) higher the risk of formation of thrombus. Similarly, patients with high D-dimer values showed increased presence of PTE, to a lesser extent ferritin showed similar association. Patients with higher CT-SS and D-dimer levels, irrespective of age and gender, with clinical suspicion of PTE should undergo CTPA. In circumstances where patient cannot undergo CTPA due to unavailability of CT or due to patient factors when there is a suspicion of PTE in severe and very severe covid disease it is safe to start therapeutic thromboprophylaxis as the risk is substantially high.

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