



# Pulmonary embolism at CT pulmonary angiography in patients with COVID-19 at a tertiary care center in Nepal: a cross-sectional study

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**Introduction:** Coronavirus disease 2019 (COVID-19) began to spread in December 2019 and was declared a pandemic by WHO on 11 March 2020. Pulmonary embolism (PE) is a known sequel to COVID-19 infection. Many patients showed worsened symptoms of thrombotic events of pulmonary arteries during the second week of the disease for which computed tomography pulmonary angiography (CTPA) is recommended. The most frequent complications in critically ill patients are prothrombotic coagulation abnormalities and thromboembolism. So, this study aimed to assess the prevalence of PE in patients with COVID-19 infection and to evaluate the relation to disease severity on CTPA findings.

**Methods:** This cross-sectional study was performed to evaluate the patients who tested positive for COVID-19 and underwent CTPA. COVID-19 infection in participants was confirmed by a PCR of nasopharyngeal or oropharyngeal swab samples. Frequencies of computed tomography severity scores and CTPA were calculated and compared with clinical and laboratory findings.

**Results:** The study included 92 patients with COVID-19 infection. Positive PE was found in 18.5% of the patients. The mean age of the patients was  $59.83 \pm 13.58$  years with an age range of 30–86 years. Among the total participants, 27.2% underwent ventilation, 19.6% died during treatment, and 80.4% of them got discharged. PE was developed in patients who did not receive prophylactic anticoagulation, which is statistically significant ( $P \leq 0.001$ ). There was also a significant relationship between mechanical ventilation and CTPA findings.

**Conclusions:** The authors conclude from their study that PE is one of the complications of COVID-19 infection. Rising D-dimer during the second week of disease alerts clinicians to do CTPA to exclude or confirm PE. This will help in the early diagnosis and treatment of PE.

**Keywords:** COVID-19, computed tomography pulmonary angiography, computed tomography severity score, pulmonary embolism

## Introductions

### Background

Coronavirus disease 2019 (COVID-19) presents as asymptomatic carriers in patients requiring assisted ventilator support<sup>[1,2]</sup>. Computed tomography (CT) is one of the main diagnostic tools for the early diagnosis and treatment of COVID-19

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## HIGHLIGHTS

- Pulmonary embolism (PE) is a known sequel to coronavirus disease 2019 (COVID-19) infection.
- Many patients showed worsened symptoms of thrombotic events of pulmonary arteries during the second week of the disease, for which computed tomography pulmonary angiography (CTPA) is recommended.
- Rising D-dimer during the second week of disease alerts clinicians to do CTPA to exclude or confirm PE.

pneumonia<sup>[3]</sup>. One of the known sequels of COVID-19 infection is pulmonary embolism (PE)<sup>[4]</sup>. Many patients showed symptoms of thrombotic events of pulmonary arteries, with worsened symptoms, especially during the second week of the disease, and for this CT pulmonary angiography (CTPA) is recommended<sup>[5]</sup>. In COVID-19 patients who have signs of clinical severity and high D-dimer levels, CTPA can be performed to rule out PE<sup>[6]</sup>. Coagulation parameters like elevated levels of D-dimer and fibrin degradation products significantly correlate with mortality in patients with COVID-19<sup>[7]</sup>. Both inflammation storm and coagulation activation caused by high D-dimer levels have been associated with increased mortality<sup>[8,9]</sup>. So, this study aimed to assess the presence of PE in patients with COVID-19 infection with severe respiratory symptoms.

**Methods**

This was a retrospective single-center cross-sectional study conducted on patients who tested positive for COVID-19 and underwent CTPA from November 2020 to April 2021. We used a census sampling method in this study. The patients were reviewed to identify those who had COVID-19 infection confirmed by PCR of nasopharyngeal or oropharyngeal swab samples. Ethical approval was taken from the Ethical Review Board of Nepal Health Research Council with reference number 681. Only the patients who tested positive for COVID-19 with PCR testing were included in the study sample. Data were first collected in a proforma by extracting them from hospital patient records and electronic medical record systems. The data were then tabulated in Microsoft Excel spreadsheets and analyzed with the help of SPSS (Statistical Package for Social Science) version 16.

The work has been reported in line with the STROCSS criteria.

**Results**

The study included 92 patients proven by PCR to have COVID-19 infection. Seventeen patients representing 18.5% of the patients, showed positive PE; among them, 18.8% (3) were female and 18.4% (14) were male. The mean age of the patients was  $59.83 \pm 13.58$  years with an age range of 30–86 years (Fig. 1). There were four (4.3%) smokers, 78 (84.8%) nonsmokers, and 10 (10.9%) ex-smoker.

COVID-19 Reporting and Data System (CO-RADS) scores were calculated. Among the total participants, 70.7% had a proven CO-RADS score, 22.8% had a very high, and 6.5% had a high CO-RADS score (Fig. 2).

Patients presented with chief complaints of Shortness of breath 84.8% (78), Cough 69.6% (64), and Fever 69.6% (64). Other complaints were chest pain, myalgia, and loose stool. The final diagnosis of participants was COVID-19, COVID-19 with mediastinal lymphadenopathy, pleural effusion, cardiomegaly, hiatal hernia, pneumomediastinum, and subcutaneous emphysema (Table 1).

The mean days of hospital stay were  $10.85 \pm 8.63$ . There were 76 patients (82.6%) males, while the rest 16 (17.4%) were female patients. The most common comorbidities among the participants were Hypertension (55.4%) followed by Diabetes (30.4%). Among the total participants, 25 (27.2%) underwent ventilation, 18 (19.6%) participants died during treatment, and 74 (80.4%) of them got discharged. However, 17 (18.5%) participants got

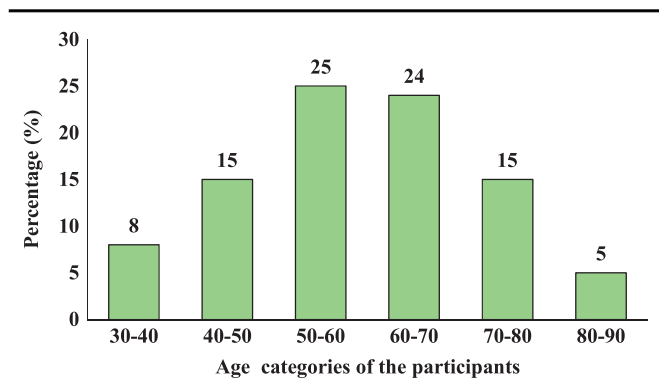


Figure 1. Age-wise distribution of the participants.

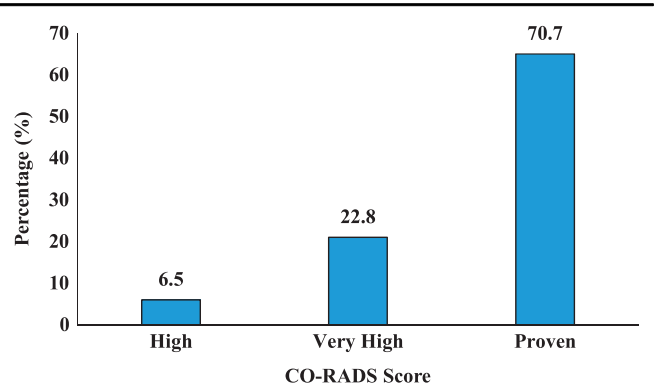


Figure 2. CO-RADS Score of the participants. CO-RADS, COVID-19 Reporting and Data System.

therapeutic anticoagulants and 75 (81.5%) got prophylactic anticoagulation.

No significant difference was found between the incidence of PE and the sex and comorbidities of the participants. Similarly, mechanical ventilation showed a statistically significant relationship with the incidence of PE, and participants who were on therapeutic and prophylactic anticoagulation showed significant relation with the incidence of PE. However, there was no significant difference between the incidence of PE and the death and discharge of the participants (Table 2).

Various laboratory investigations were done. Among the total participants, 63% (58) had high D-dimer with 29.3% (17) positive CTPA, which showed a significant relationship with the incidence of PE. There were a total of 90 (97.8%) participants who had high lactate dehydrogenase (LDH), 36 (39.1%) had high total leukocyte count (TLC), and 73 (79.3%) had high neutrophil count. However, 80.4% (74) had low lymphocytes count. Likewise, 81.5% (75) of participants had high ferritin levels and 96.7% (89) had high CRP levels, and 41.3% (38) had high activated partial thromboplastin clotting time (APTT). Regarding the prothrombin count (PT) and international normalized ratio (INR), 12% (11) had high PT and 10.9% (10) had high INR levels, which showed a significant relationship with the incidence of PE (Table 3).

Regarding the CT severity score (CTSS), 62.5% (10) of females and 77% (59) of males had severe CT scores. Of those participants who had comorbidities like Hypertension, 74.5% (38) and Diabetes, 85.7% (24) had severe CTSS. Of those participants who were on mechanical ventilation, 92% (23) had severe CTSS

**Table 1**

**Final diagnosis of the participants**

Final diagnosis	Frequency (N)	Percent (%)
COVID-19	64	69.6
COVID-19 with mediastinal lymphadenopathy	11	12
COVID-19 with pleural effusion	5	5.4
COVID-19 with cardiomegaly	4	4.3
COVID-19 with hiatal hernia	3	3.3
COVID-19 with pneumomediastinum	2	2.2
COVID-19 with subcutaneous emphysema	2	2.2

COVID-19, coronavirus disease 2019.

**Table 2**  
**Clinical characteristics of patients with COVID-19 who had diagnostic chest CTPA and differences in clinical features between patients with positive and negative CTPA**

Clinical characteristics	All patients (n=92), N (%)	CTPA negative (n=75), N (%)	CTPA positive (n=17), N (%)	P
Sex				
Female	16 (17.4)	13 (81.3)	3 (18.8)	0.97
Male	76 (82.6)	62 (81.6)	14 (18.4)	
Comorbidities				
Hypertension	51 (55.4)	41 (80.4)	10 (19.6)	0.75
Diabetes	28 (30.4)	24 (85.7)	4 (14.3)	0.49
COPD	5 (5.4)	4 (4.3)	1 (1.1)	0.92
DVT	3 (3.3)	3 (3.3)	–	0.40
CAD	3 (3.3)	3 (3.3)	–	0.40
Stroke	2 (2.2)	2 (2.2)	–	0.49
Clinical outcomes				
Mechanical ventilation	25 (27.2)	17 (68)	8 (32)	0.04
Discharge	74 (80.4)	63 (85.1)	11 (14.9)	0.07
Death	18 (19.6)	12 (66.7)	6 (33.3)	0.07
Anticoagulation therapeutic	17 (18.5)	–	17 (100)	<0.001
Anticoagulation prophylactic	75 (81.5)	75 (100)	–	<0.001

CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; CTPA, computed tomography pulmonary angiography; DVT, deep vein thrombosis.

which were also statistically significant. Among the total participants, 71.6% (53) who were discharged and 88.9% (16) who were deceased had severe CTSS. Of all the participants who were on therapeutic anticoagulants, 100% (17) and 69.3% (52) of participants who were on prophylactic anticoagulants had severe CTSS and this showed a significant relationship with each other (Table 4).

Among the total participants who had high D-dimer, 64.7% (22) had severe CTSS and among those who had high LDH, 74.4% (67) had severe CTSS. Likewise, regarding participants who had high TLC, 77.8% (28) had severe CTSS and for those with a high neutrophil count, 80.8% (59) had severe CTSS. Similarly, 77.3% (58) of participants who had high ferritin and 74.2% (66) who had high C-reactive protein (CRP) had severe CTSS. Among those participants who had low lymphocyte count, 50% (2) had severe CTSS which were also statistically significant. Of the participants who had high PT, INR, and APTT, among them 63.6% (7), 90% (9), and 76.3% (29) had severe CTSS respectively (Table 5).

**Discussions**

Respiratory tract infection is considered a risk factor in the development of PE, especially in hospitalized patients<sup>[10]</sup>. This study revealed that the incidence of PE in patients with COVID-19 who underwent CT pulmonary angiography was reported to be 18.5%. These findings were similar to the findings of the study done in the USA and France, Poyiadji *et al.*<sup>[11–13]</sup>. But in contrast the study done in New York by Kaminetzky *et al.*<sup>[14]</sup> shows there were 37.1% of positive cases for PE. Also, the study done in Italy, the UK, and Madrid and the study done by Middeldorp *et al.* revealed that PE ranges from 2.8 to 6.6%<sup>[15–18]</sup>.

**Table 3**  
**Differences in laboratory values between patients with positive and negative chest CTPA**

Laboratory values	All patients (n=92), N (%)	CTPA negative (n=75), N (%)	CTPA positive (n=17), N (%)	P
D-dimer				
Normal	34 (37)	34 (100)	–	<0.001
High	58 (63)	41 (70.7)	17 (29.3)	
LDH				
Normal	2 (2.2)	2 (100)	–	0.49
High	90 (97.8)	73 (81.1)	17 (18.9)	
TLC				
Low	7 (7.6)	7 (100)	–	0.12
Normal	49 (53.3)	42 (85.7)	7 (14.3)	
High	36 (39.1)	26 (72.2)	10 (27.8)	
Neutrophil				
Low	2 (2.2)	2 (100)	–	0.56
Normal	17 (18.5)	15 (88.2)	2 (11.8)	
High	73 (79.3)	58 (79.5)	15 (20.5)	
Lymphocytes				
Low	74 (80.4)	60 (81.1)	14 (18.9)	0.83
Normal	18 (19.6)	15 (83.3)	3 (16.7)	
Ferritin				
Low	4 (4.3)	3 (75)	1 (25)	0.54
Normal	13 (14.1)	12 (92.3)	1 (7.7)	
High	75 (81.5)	60 (80)	15 (20)	
CRP				
Normal	3 (3.3)	2 (66.7)	1 (33.3)	0.50
High	89 (96.7)	73 (82)	16 (18)	
PT				
Low	2 (2.2)	2 (100)	–	0.04
Normal	79 (85.9)	67 (84.8)	12 (15.2)	
High	11 (12)	6 (54.5)	5 (45.5)	
INR				
Low	1 (1.1)	1 (100)	–	0.02
Normal	81 (88)	69 (85.2)	12 (14.8)	
High	10 (10.9)	5 (50)	5 (50)	
APTT				
Low	7 (7.6)	5 (71.4)	2 (28.6)	0.59
Normal	47 (51.1)	40 (85.1)	7 (14.9)	
High	38 (41.3)	30 (78.9)	8 (21.1)	

APTT, activated partial thromboplastin clotting time; CRP, C-reactive protein; CTPA, computed tomography pulmonary angiography; INR, international normalized ratio; LDH, lactate dehydrogenase; PT, prothrombin count; TLC, total leukocyte count.

The mean age of the patients was 59.83 ± 13.58 years with an age range of 30–86 years, according to this study’s findings. This was in concordance with the findings of the study done by Kaminetzky *et al.*<sup>[14]</sup> and a study done in the UK<sup>[18]</sup>. According to this study, patients present with chief complaints of Shortness of breath, Cough, and Fever. This was relatively similar to the findings of the study conducted in Egypt and Italy<sup>[4,19]</sup>. The most common comorbidities among the participants were Hypertension (55.4%) followed by Diabetes (30.4%). Likewise, these findings were supported by the study done in New York, USA<sup>[14]</sup>.

Among the total participants, 27.2% underwent ventilation, 19.6% of participants died during treatment, and 80.4% of them got discharged. This was in agreement with the findings of the study done in New York, USA<sup>[14]</sup>. However, 18.5% of participants got therapeutic anticoagulants, and 81.5% got prophylactic anticoagulation, which was in contrast to the study done by Kaminetzky *et al.*<sup>[14]</sup> in New York, which showed that only 40%

**Table 4**  
**Clinical characteristics of patients with COVID-19 and differences in clinical features between patients with mild–moderate CTSS and severe CTSS**

Clinical characteristics	All patients (n=92), N (%)	CT score (mild–moderate) (n=23), N (%)	CT score (severe) (n=69), N (%)	P
Sex				
Female	16 (17.4)	6 (37.5)	10 (62.5)	0.20
Male	76 (82.6)	17 (22.4)	59 (77.6)	
Comorbidities				
Hypertension	51 (55.4)	13 (25.5)	38 (74.5)	0.90
Diabetes	28 (30.4)	4 (14.3)	24 (85.7)	0.11
COPD	5 (5.4)	4 (4.3)	1 (1.1)	0.003
DVT	3 (3.3)	2 (2.2)	1 (1.1)	0.09
CAD	3 (3.3)	1 (1.1)	2 (2.2)	0.73
Stroke	2 (2.2)	–	2 (2.2)	0.40
Clinical outcomes				
Mechanical ventilation	25 (27.2)	2 (8)	23 (92)	0.02
Discharge	74 (80.4)	21 (28.4)	53 (71.6)	0.12
Death	18 (19.6)	2 (11.1)	16 (88.9)	0.12
Anticoagulation therapeutic	17 (18.5)	–	17 (100)	0.008
Anticoagulation prophylactic	75 (81.5)	23 (30.7)	52 (69.3)	0.008

CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; CT, computed tomography; DVT, deep vein thrombosis.

of patients receiving a prophylactic dose of anticoagulation. Statins have been previously described to be associated with decreased rates of venous thromboembolism, as well as decreased risk of recurrent PE<sup>[20,21]</sup>.

Similarly, mechanical ventilation showed a statistically significant relationship with the incidence of PE, and participants who were on therapeutic and prophylactic anticoagulation showed significant relation with the incidence of PE. These findings were in line with the results from a study done in China and Kollias *et al.*, which showed that there had been an association between COVID-19-positive patients who are diagnosed with PE and treatment with anticoagulation prophylaxis, such as low molecular weight heparin<sup>[22,23]</sup>. However, there was a high rate of PE (52%) in COVID-19-positive patients who were receiving prophylactic anticoagulation and were shown to decrease mortality according to the study done in China and the USA<sup>[24]</sup>. But, there was no significant difference between the incidence of PE and the death and discharge of the participants in this study's findings.

No significant difference was found between the incidence of PE and the sex and comorbidities of the participants. This was similar to the findings of the study done by Kaminetzky *et al.*<sup>[14]</sup> and a study done in the UK<sup>[18]</sup>. Among the total participants, 63% had high D-dimer with 29.3% positive CTPA, which showed a significant relationship with the incidence of PE. Likewise, the various studies done in Spain, the USA, the UK, and France showed that the D-dimer level was higher among the PE-positive group relative to the PE-negative group<sup>[14,18,25,26]</sup>. Also, other studies were done by Mestre-Gómez *et al.*<sup>[17]</sup>, Poyiadji *et al.*<sup>[13]</sup>, and Wallace *et al.*<sup>[20]</sup> showed that D-dimer values were significantly higher in PE patients. The study done in Wuhan, China, revealed that increased D-dimer levels have been

**Table 5**  
**Differences in laboratory values between patients with mild–moderate CTSS and severe CTSS**

Laboratory values	All patients (n=92), N (%)	CT score (mild–moderate) (n=23), N (%)	CT score (severe) (n=69), N (%)	P
D-dimer				
Normal	34 (37)	12 (35.3)	22 (64.7)	0.08
High	58 (63)	11 (19)	47 (81)	
LDH				
Normal	2 (2.2)	0	2 (100)	0.40
High	90 (97.8)	23 (25.6)	67 (74.4)	
TLC				
Low	7 (7.6)	3 (42.9)	4 (57.1)	0.51
Normal	49 (53.3)	12 (24.5)	37 (75.5)	
High	36 (39.1)	8 (22.2)	28 (77.8)	
Neutrophil				
Low	2 (2.2)	1 (50)	1 (50)	0.04
Normal	17 (18.5)	8 (47.1)	9 (52.9)	
High	73 (79.3)	14 (19.2)	59 (80.8)	
Lymphocytes				
Low	74 (80.4)	15 (20.3)	59 (79.7)	0.03
Normal	18 (19.6)	8 (44.4)	10 (55.6)	
Ferritin				
Low	4 (4.3)	2 (50)	2 (50)	0.41
Normal	13 (14.1)	4 (30.8)	9 (69.2)	
High	75 (81.5)	17 (22.7)	58 (77.3)	
CRP				
Normal	3 (3.3)	0	3 (100)	0.30
High	89 (96.7)	23 (25.8)	66 (74.2)	
PT				
Low	2 (2.2)	0	2 (100)	0.48
Normal	79 (85.9)	19 (24.1)	60 (75.9)	
High	11 (12)	4 (36.4)	7 (63.6)	
INR				
Low	1 (1.1)	0	1 (100)	0.42
Normal	81 (88)	22 (27.2)	59 (72.8)	
High	10 (10.9)	1 (10)	9 (90)	
APTT				
Low	7 (7.6)	1 (14.3)	6 (85.7)	0.72
Normal	47 (51.1)	13 (27.7)	34 (72.3)	
High	38 (41.3)	9 (23.7)	29 (76.3)	

APTT, activated partial thromboplastin clotting time; CRP, C-reactive protein; CT, computed tomography; INR, international normalized ratio; LDH, lactate dehydrogenase; PT, prothrombin count; TLC, total leukocyte count.

associated with increased mortality in adult patients with COVID-19<sup>[9]</sup>.

This study revealed that there were 82.6% of male while the rest (17.4%) were female patients. This was consistent with the study done in New York, which shows that patients who had COVID-19 comprised a significantly higher fraction of men, which may result from men associated with worse prognoses and higher mortality<sup>[14]</sup>. It has also been reported in the literature from Wuhan, China, that the severity of disease with COVID-19 infection was more in men than in women<sup>[27]</sup>.

CTSSs were higher among the severe category versus the mild–moderate category. This was in concordance with the findings from the study done in Egypt<sup>[4]</sup>. Among those participants who had low lymphocyte count, 50% had severe CT scores which were also statistically significant. This finding was in line with the results of earlier studies published in Wuhan, China<sup>[28]</sup>.

## Conclusions

We conclude from our study that PE is one of the complications of COVID-19 infection. Rising D-dimer during the second week of disease, which all are alert to do CT pulmonary angiography to exclude or confirm PE. This will help in the early diagnosis and treatment of PE in the future. The incidence of PE and COVID-19 disease severity, either by laboratory or by the CTSS, will help in the early anticipation, diagnosis, and treatment of complicated COVID-19 infection cases.

## Limitation

The study was conducted at a single-center health institution; thus, it may not be generalizable to the entire country.

## Ethical approval

Taken from Nepal Health Research Council (Reference Number: 681).

## Consent

Written informed consent was obtained from the patient. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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None.

## Author contribution

I.A.: study concept, designing, literature review, data analysis, and interpretation of the results and writing in I.A.; P.R.R.: study designing, data analysis, and interpretation of the results; B.P., G.A., A.B., and A.D.: data collection and writing the paper. All authors were involved in manuscript drafting and revising, and approved the final version.

## Conflicts of interest disclosure

None of the authors have conflicts of interest for this study.

## Research registration unique identifying number (UIN)

1. Name of the registry: not applicable.
2. Unique identifying number or registration ID: not applicable.
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): not applicable.

## Guarantor

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## Provenance and peer review

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