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The prevalence of pulmonary embolism in COVID-19 patients using computed tomography pulmonary angiography

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An elevated occurrence of abnormal coagulation variables and pulmonary embolism (PE) has been noted since the initiation of the COVID-19 pandemic, especially in the case of critically ailing individuals who need intensive care unit (ICU) admission. This research was conducted to evaluate the prevalence of PE using CT pulmonary angiography (CTPA) in individuals diagnosed with COVID-19.This retrospective study evaluated 156 COVID-19 individuals who had CTPA between April 16th, 2022, and March 25th, 2023, for clinical suspicion of PE. Clinical outcomes and laboratory tests were additionally examined and correlated with the existence of disease severity and pulmonary embolism (PE).A total of 156 individuals with confirmed COVID-19 and severe clinical features underwent CTPA examination. A total of 102 men (65%) had a median age of 54 years, and 54 women (35%) had a median age of 56 years [interquartile range (IQR): 39-71 years](Table 1). Among the 156 patients who underwent CTPA examination, 33 patients had acute pulmonary embolism (Figure 1)(21.1%, [95% CI, 15-33%].The findings of this research reveal that approximately one-fifth of COVID-19 pneumonia patients, who underwent evaluation post-contrast administration, exhibited acute pulmonary embolism on CT scans. This underscores the notable incidence of pulmonary embolism among individuals with severe COVID-19 pneumonia.

Keywords: Corona virus disease 2019(COVID-19), CT pulmonary angiography (CTPA), pulmonary embolism (PE),Venous thromboembolism (VTE)

INTRODUCTION

Several healthcare facilities in Wuhan, Hubei Province, China, documented instances of patients with pneumonia of unidentified originaetiology at the end of December 2019. Epidemiological evidence linked these patients to a seafood as well as wet animal wholesale market (Zhu, et al. 2020, Olié, et al. 2021). Subsequently, CT imaging has become more widespread in the diagnosis and monitoring of this disorder, and there is a growing understanding of the radiological patterns observed throughout the progression of the disease (Rotzinger et al. 2020, Boussouar et al. 2020). As the disease spreads, there has been an observed increase in aberrant blood coagulation factors, leading to a higher occurrence of venous thromboembolic (VTE) consequences (Klok et al. 2020, Akel et al. 2020). Recent findings have emphasised the high frequency of blood clotting events in patients in the intensive care unit (ICU)(Klok et al. 2020). Respiratory viruses are thought to have a significant impact on the process of blood clot formation, known as the coagulation cascade (Akel et al. 2020, Mohamud and Mukhtar 2022). Previous studies have documented the occurrence of VTEs and hypercoagulability in severe respiratory tract infections, including influenza (Obi et al. 2019, Dimakakos et al. 2016). In vitro infection of cultivated human endothelial cells by respiratory viruses has been shown to induce a pro-coagulant condition (Visseren et al.2000). Recent literature includes a limited number of investigations and isolated clinical instances discussing COVID-19 pneumonia accompanied by pulmonary embolism and coagulopathy (Grillet et al. 2020). Sudan, the second-largest nation in Africa with an estimated population of 43,849,260, is also impacted by the worldwide COVID-19 pandemic. The first instance of the new coronavirus was documented in Khartoum on March 13, 2020. The person, who had travelled to the United Arab Emirates in early March, passed away from the illness on March 12, 2020 (Alah Abdeen, and Kehyayan, 2020). In light of the

COVID-19 pandemic, the Federal Ministry of Health (FMH) in Sudan instituted a Health Emergency Committee (HEC)(Musa et al. 2020). The FMH, along with other governmental and civilian organisations, formulated COVID-19 case management standards to facilitate the identification, diagnosis, and treatment of individuals suspected to have the virus. The total number of confirmed cases reached 33,648, with 2,365 virus-related deaths in the whole country by the 8th of May 2021. (https://www.worldometers.info/coronavirus/Accessed on 9 May 2021).

The primary objective of this study is to examine the relationship between PE and COVID-19 infection among Sudanese patients diagnosed using CTPA. Furthermore, the study seeks to examine potential connections between the severity of COVID-19, blood D-dimer (DD) levels, and the occurrence of pulmonary thromboembolism (PTE).

MATERIALS AND METHODS

In this retrospective study, we conducted a review of CT pulmonary angiographies (CTPA) for 156 patients diagnosed with COVID-19 between April 16th, 2022, and March 25th, 2023, in Khartoum Province hospitals. Ethical approval for the study was obtained from the Research Ethics Committee at the University of Khartoum. Given that the study was retrospective in nature, the committee decided to waive the requirement for written informed consent, the de identification of data, and the absence of any potential risk to the patients. To ensure confidentiality, no identifiable link between the authors and the patients was established. The authors declare no conflicts of interest related to this study.

Inclusion criteria for the study encompassed adult patients with confirmed COVID-19 positivity through corona virus polymerase chain reaction (PCR) testing of nasopharyngeal or or pharyngeal swab specimens. CTPA examinations were conducted in cases of sudden severe clinical deterioration or rapidly worsening dyspnea.

CTPA procedures were conducted utilizing an 80-slice CT scanner (Somatom Definition, Siemens Medical Solutions, Germany) with a tube voltage set at 140/80 kVp and tube current at 51/213 m As.The rotation time was 0.33 s, and the scan produced 0.75 mm-thick slices with a reconstruction increment of 0.7. The patients underwent scanning while in a supine position, covering the lung area from apex to diaphragm. Contrast enhancement was achieved by injecting a bolus of non-ionic contrast medium (iomeprol 350 mg/mL) at a rate of at least 3.5 mL/s, followed by a 30 mL rapid saline solution flush at a minimum flow rate of 3 mL/s.

Two radiologists, each with 11 and 12 years of experience, independently conducted radiological assessments of COVID-19 features on chest CT scans and examined the presence of pulmonary embolism. The radiologists were blinded to patient status and clinical features. Simultaneous readings were conducted for suspicious cases to reach a consensus. The degree of pulmonary vessel obstruction was evaluated using the Mastora obstruction scoring system (Xu et al. 2020), categorizing obstruction as follows: less than 25% (graded as 1), 25-49% (graded as 2), 50-74% (graded as 3), 75-99% (graded as 4), and 100% (graded as 5). Assessment of pulmonary opacities related to COVID-19 employed an adapted scoring system (D'Elia et al. 2021), scoring each of the six lung lobes based on the percentage involvement: less than 25% (scored 1), 25-50% (scored 2), 50-75% (scored 3), and 75-100% (scored 4). D-dimer levels were obtained as close as possible to the CTA date.

Statistical Analysis

All relevant information regarding the study data was extracted from the Electronic Patient Record (EPR) system. This encompassed details such as the indication for the CTPA request, the number of days of hospital admission at the time of CTPA examination, D-dimer levels, and the categorization of patients as either ward or ICU patients, with or without mechanical ventilation.

In order to determine the clinical characteristics linked to pulmonary embolism, prospective independent variables such as the severity of lesions observed on CT scans, the need for mechanical ventilation, co morbidities, and demographic information were taken into consideration and analysed using a logistic regression model. A significance level of $P < 0.05$ was used to denote statistical significance. All analyses were conducted using descriptive statistics with the Statistical Package for Social Science computer program (SPSS Inc., Chicago, IL, USA), version 25.

RESULTS

A total of 156 individuals with confirmed COVID-19 and serious clinical characteristics underwent CTPA examination. A total of 102 men (65%) had a median age of 54 years, and 54 women (35%) had a median age of 56 years [interquartile range (IQR): 39-71 years](Table 1). Among the 156 patients who underwent CTPA examination, 33 patients had acute pulmonary embolism (Figure 1)(21.1%, [95% CI, 15-33%]).

Documented clinical indications in the medical record for the CTPA examination for the 156 COVID-19 patients were as follows: respiratory distress in 50 (32%), hypoxia in 39 (25%), chest pain in 31 (19.9%), tachycardia in 19 (12.2%), and hypotension in 17 (10.9%) (Figure 2).

Table 1: Age and gender distribution among COVID-19 PE positive vs PE negative patients

	Total (SD)	Positive PE on CTPA (SD)	Negative PE on CTPA (SD)	p value
	N = 156	N = 33	N = 123	
Total Age	55 ± 11	57 ± 11	54 ± 11	.80
Male Age	56 ± 8	58 ± 8	56 ± 8	.80
Female Age	54 ± 9	55 ± 9	54 ± 9	.80

SD = standard deviation

Table 2: Care status, *Invasive* mechanical ventilation, and Time of CTPA of COVID-19 PE positive vs PE negative patients and time of CTPA from onset of symptoms

Care status	Total (%)	Positive PE on CTPA (%)	Negative PE on CTPA (%)	p value
	N = 156	N = 33	N = 123	
Conventional care	111 (71%)	6 (18%)	105 (85%)	<.001
Critical care	45(29%)	27 (82%)	18 (14%)	<.001
Invasive mechanical Ventilation	39 (25%)	15 (45%)	12 (9%)	<.001

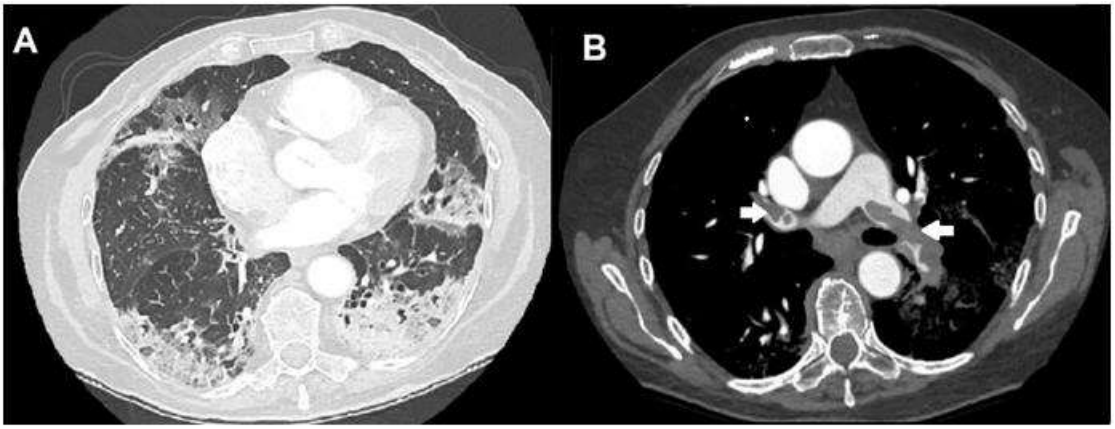

Figure 1: A 64-year-old male with COVID-19 with acute pulmonary embolism. *A:*CT-Scan; axial unenhanced lung window: show bilateral peripheral ground-glass opacity, associated with crazy paving and consolidation .*B:*axial CT-Scan angiography media stinal window demonstrates filling defects (white arrows)inside right and left main pulmonary arteries, indicates pulmonary embolism (PE)

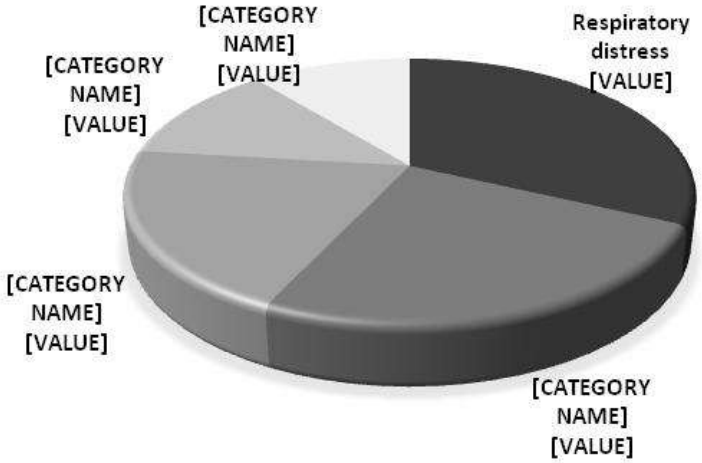

Figure 2: Clinical indications for the CTPA examination

Table 3: Comorbidities Associated among COVID-19 PE positive vs PE negative patients:

Co morbidities	Total (%)	Positive PE on CTPA (%)	Negative PE on CTPA (%)	p value
	N = 156	N = 33	N = 123	
Diabetes (type II)	147 (94%)	30 (91%)	117 (95%)	.81
Cardiovascular disease	60 (38%)	18 (54%)	42 (34%)	.55
Malignancy	45 (29%)	12 (36%)	33 (27%)	.39

Patients with PE were more frequently hospitalized in the ICU than those without PE (27/33 (81.8%) vs 18/123 (14.6%) patients, P<0.001), with more frequent mechanical ventilation (15/33 (45.4%) vs 12/123 (9.7%) and a longer median duration of hospital admission (45 [9 - 17] versus 24 [4 - 12] days, P=0.04)(Table 2). PE positive patients had a significantly high mean D-dimer level (p = 0.001).Median D-dimer values was 6441 mcg/L (range 219, 90925).

The most common associated co morbidity was type II diabetes (94%), followed by cardiovascular diseases (38%) and malignancy (29%) (Table 3). Regarding the outcome, there were 6 deaths in the PE-positive patients (6/33, 18.1%), and no deaths were reported in the PE-negative group.

DISCUSSION

Our study revealed that COVID-19 is associated with 21% of acute pulmonary embolisms. CTPA examinations revealed a significant difference in D-dimer levels between patients with and without PE (Calabrese, C., et al.2021, Mueller-Peltzer, K., et al. 2020).The elevated incidence of PE observed in our study of COVID-19 patients is consistent with growing evidence that emphasises the growing correlation between COVID-19 and hypercoagulable conditions, such as disseminated intravascular coagulation.

A similar study performed by Grillet et al. in Besançon, France, between March 15th and April 14th among 100 patients with COVID-19 showed that 23% of these patients were diagnosed with acute pulmonary embolism, which was similar to our study findings (Grillet et al.2020, Xu et al. 2020, D'Elia et al. 2021). Our findings were also in line with an observational study performed at the Henry Ford Health System's hospitals in Detroit between March 16th and April 18th, which showed that PE was observed in 22% of 328 COVID-19 patients who underwent pulmonary CT angiography. Visseren et al. demonstrated the ability of respiratory viruses to induce pro-coagulant activity in infected lung fibroblasts and human umbilical vein endothelial cells in culture by reducing the clotting time by approximately 55%(Visseren et al. 2000, Collange et al. 2020).

The more the COVID-19 pandemic continues to progress, the more we learn about coagulation disorders and the dysregulation of haemostatic pathways that occurs in the disease (Gallastegui et al. 2021 , Jayakrishnan et al. 2021). It is hypothesized that inflamed lung parenchyma and pulmonary vascular endothelium may lead to increased release of procoagulant factors, which will induce a coagulation cascade, leading to fibrin deposition and thrombus formation within pulmonary vessels (Xu et al. 2020).

Y J Suh et al. conducted a meta-analysis regarding the incidence of PE and DVT at the study level. Furthermore, the diagnostic precision of D-dimer assays for PE was evaluated by analysing patient-specific data from multiple centres. It was observed that patients admitted to the intensive care unit had a greater incidence of PE. Patients who were not admitted to the intensive care unit had DVT at a rate of 24.7%, whereas in studies employing universal screening with CT pulmonary angiography, 42.4% of patients with PE had DVT (Suh et al. 2020). According to their findings (Suh et al. 2021), PE and DVT were identified in 16.5% and 14.8% of patients infected with COVID-19, respectively.

A study performed by Tang et al. 2020 showed that decreased mortality among COVID 19 patients is strongly associated with initial treatment with anticoagulants.

For COVID-19 pneumonia patients exhibiting limited disease extension, the European Society of Radiology and the European Society of Thoracic Imaging issued an advisory recommending the utilization of contrast-enhanced CT when supplemental oxygen is necessary to assess and rule out PE (Goeijenbier et al.2012). Patients diagnosed with COVID-19 have high risk factors for pulmonary embolus; therefore, CTPA is advised as a standard practice for individuals exhibiting severe clinical manifestations of COVID-19 to assess potential complications leading to respiratory distress and to examine the lung parenchyma (Bakirli et al. 2021). PE-positive patients were more likely to require ICU care and mechanical ventilation than PE-negative patients.

CONCLUSIONS

In conclusion, acute pulmonary embolism was identified on CT scans of nearly one-fifth of COVID-19 pneumonia patients who underwent evaluation subsequent to contrast administration. This indicates that PE is prevalent among patients with severe

pneumonia caused by COVID-19. As a result, it is critical that a greater quantity of contrast be utilised during thoracic CT examinations of patients with COVID-19 pneumonia. It is recommended that hospitalised patients with COVID-19 pneumonia be prophylactically treated with low-molecular-weight heparin in order to mitigate the risk of thromboembolism complications.

Supplementary materials
The supplementary material / supporting for this article can be found online and downloaded at: https://www.isisn.org/article/

CONFLICT OF INTEREST
The authors declared that present study was performed in absence of any conflict of interest.

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AUTHOR CONTRIBUTIONS
All author contributed in all parts of the paper.

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Not applicable.

Data Availability Statement
All of the data is included in the article/Supplementary Material.

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Conflict of interest
The authors declared that present study was performed in absence of any conflict of interest.
OR The authors declare no conflict of interest.

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REFERENCES

Alah MA, Abdeen S, and V. Kehyayan, The first few cases and fatalities of Corona Virus Disease 2019 (COVID-19) in the Eastern Mediterranean Region of the World Health Organization: A rapid re*view.* Journal of Infection and Public Health, 2020.

Akel T, Qaqa F, Abuarqoub A, Shamoon F. *Pulmonary embolism: a complication of COVID 19 infection.* Thrombosis research, 2020. 193: p. 79-82.

Bakirli, I., et al. *Symptomatic carotid artery thrombosis in a patient recently recovered from a COVID-19 infection.* Cureus, 2021. 13(10).

Boussouar S, Wagner M, Donciu V, Pasi N, Salem JRenard-Penna R, Marot S, Freund Y, Redheuil A and Lucidarme O. Diagnostic performance of chest computed tomography during the epidemic wave of COVID-19 varied as a function of time since the beginning of the confinement in France. PloS one, 2020. 15(11): p. e0242840.

Calabrese C, Annunziata A, Coppola A, Pafundi P, Guarino S, Di Spirito V, Maddaloni V, Pepe N, Fiorentino G. ACE gene I/D polymorphism and acute pulmonary embolism in COVID19 pneumonia : a potential predisposing role. Frontiers in medicine, 2021. 7: p. 631148.

Collange O, Tacquard C, Delabranche X, Leonard-Lorant I, Ohana M, Onea M, Anheim M, Solis M, Sauer A, Baloglu S. Coronavirus disease 2019: associated multiple organ damage. in Open forum infectious diseases. 2020. Oxford University Press US.

D'Elia E, Gori M, Grosu A, Iorio A, Lorini F, Falanga ADi Marco F, Senni M. An unexpected case of recurrence of pulmonary embolism in a patient recovered from COVID19 in full regimen dose of direct oral anticoagulant drug. BMC Pulmonary Medicine, 2021. 21: p. 1-4.

Dimakakos E, Grapsa D, Vathiotis I, Papaspiliou A,Panagiotarakou M, Manolis E, Syrigos K. H1N1-induced venous thromboembolic events? Results of a single-institution case series. in Open forum infectious diseases. 2016. Oxford University Press.

Gallastegui N, Zhou J, Drygalski A, Barnes R, Fernandes T, Morris T. Pulmonary embolism does not have an unusually high incidence among hospitalized COVID19 patients. Clinical and Applied Thrombosis/Hemostasis, 2021. 27: p. 1076029621996471.

Grillet F, Behr, Julien C, Paul A, Sébastien D. Acute pulmonary embolism associated with COVID-19 pneumonia detected with pulmonary CT angiography. Radiology, 2020. 296(3): p. E186-E188.

Goeijenbier M, Van M, Van C, Jong E, Gerdes V, Meijers J, Brandjes D, Van E. Viral infections and mechanisms of thrombosis and bleeding. Journal of medical virology, 2012. 84(10): p. 1680-1696.

Jayakrishnan T, Haag A, Mealy S, Minich C, Attah A, Turk M, Alrifai N, Alhuneafat L, Khoury F, Nasrullah A. *Novel Coronavirus Infection (COVID-19) Related Thrombotic and Bleeding Complications in Critically Ill Patients: Experience from an Academic Medical Center.* Journal of Clinical Medicine, 2021. 10(23): p. 5652.

Klok FA, Kruip M, Van der Meer N, Arbous MGommers D, Kant K, Kaptein F, Van Paassen J, Stals M Incidence of thrombotic complications in critically ill ICU patients with COVID-19. Thrombosis research, 2020. 191: p. 145-147.

Musa TH, El-Bingawi HM, Musa IH, Mohammed LAArbab M, Musa H. *Covid-19 in Sudan: Response towards control and prevention.* Medical Journal of Malaysia, 2020. 75(4).

Mueller-Peltzer K, Krauss T, Benndorf M, Lang C Bamberg F, Bode C, Duerschmied D, Staudacher D,Zotzmann V. *Pulmonary artery thrombi are co-located with opacifications in SARS-CoV2 induced ARDS.* Respiratory medicine, 2020. 172: p. 106135.

Mohamud, m.f.y. And m.s. Mukhtar, *Epidemiological characteristics, clinical relevance, and risk factors of thromboembolic complications among patients with COVID-19 pneumonia at A teaching hospital: Retrospective observational study.* Annals of Medicine and Surgery, 2022. 77: p. 103660.

Obi A, Tignanell C, Jacobs B, Arya S, Park P, Wakefield T, Henke P, Napolitano L. Empirical systemic anticoagulation is associated with decreased venous thromboembolism in critically ill influenza A H1N1 acute respiratory distress syndrome patients. Journal of Vascular Surgery: Venous and Lymphatic Disorders, 2019. 7(3): p. 317-324.

Olié V, Thiam M, Carcaillon-Bentata L, Haeghebaert S, Forgeot C, Fouillet A, Gallay A, Caserio-Schönemann C. Impact of covid19 crisis on the emergency management of cardiovascular diseases. Archives of Cardiovascular Diseases Supplements, 2021. 13(1): p. 155.

Rotzinger DC, Beigelman-Aubry C, Von Garnier C Qanadli S. Pulmonary embolism in patients with COVID-19: time to change the paradigm of computed tomography. Thrombosis research, 2020. 190: p. 58-59.

Suh Y, Hong H, Ohana M, Bompard F, Revel Marie-Pierre, Valle C, Gervaise A, Poissy J, Susen S, Hékimian G. Pulmonary Embolism and Deep Vein Thrombosis in COVID-19: A Systematic Review and Meta-Analysis. Radiology, 2020: p. 203557.

Suh Y, Hong H, Ohana M, Bompard F, Revel Marie-Pierre, Valle C, Gervaise A, Poissy J, Susen S, Hékimian G. Pulmonary embolism and deep vein thrombosis in COVID-19: a systematic review and meta-analysis. Radiology, 2021. 298(2): p. E70-E80.

Tang N, Bai H, Chen X, Gong J, Li D, Sun Z. Anticoagulant treatment is associated with decreased mortality in severe coronavirus disease 2019 patients with coagulopathy. Journal of thrombosis and haemostasis, 2020. 18(5): p. 1094-1099.

Visseren F, Bouwman J, Bouter K, Diepersloot R,De G, Ph G, Erkelens D .Procoagulant activity of endothelial cells after infection with respiratory viruses. Thrombosis and haemostasis, 2000. 84(08): p. 319-324.

Xu H, Martin A, Singh A, Narasimhan M, Lau J, Weinberg M, Jauhar R, Rao G. Pulmonary embolism in patients hospitalized with COVID-19 (from a New York health system). The American journal of cardiology, 2020. 133: p. 148-153.

Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, Zhao X, Huang B, Shi W, Lu R. A novel coronavirus from patients with pneumonia in China, 2019. New England journal of medicine, 2020.