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Radiological assessment of pulmonary vascular changes and gastrointestinal changes in COVID-19 patients referred to a tertiary health care center in Chennai, India: A prospective cross-sectional study

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ABSTRACT

Background. The COVID-19 pandemic, caused by the SARS-CoV-2 virus, has led to significant morbidity and mortality worldwide since its emergence in 2019. While primarily a respiratory illness, COVID-19 can also affect other organ systems, including the vascular and gastrointestinal systems. COVID-19 infection is linked to both venous and arterial thrombosis, with numerous studies indicating a heightened risk of pulmonary embolism (PE) among patients. Autopsies have revealed pulmonary vasculature thrombosis and bowel ischemia in COVID-19 cases.

Aim. This prospective cross-sectional study aimed to assess radiological pulmonary vascular changes, specifically pulmonary embolism (PE), and gastrointestinal changes in COVID-19 patients referred to a tertiary healthcare center in Chennai, India.

Methods. CT pulmonary angiography (CTPA) and contrast-enhanced CT of the abdomen were conducted in 100 COVID-19 positive patients meeting the inclusion and exclusion criteria. Evaluation of pulmonary vascular changes and bowel changes was performed by a radiologist with five years of experience. Subsequently, statistical analysis was carried out to determine the significance of the relationship between COVID-19 patients and the occurrence of pulmonary vascular and bowel changes.

Results. In our study, 11 patients exhibited pulmonary thromboembolism, and 7 patients showed significant bowel changes. There is a positive correlation between the prevalence of PE in COVID-19 patients. PE was diagnosed at a mean of 11 days from the onset of the disease. Out of 24 patients with severe acute respiratory illness (SARI), 7 showed PE in CTPA. Additionally, out of 10 mechanically ventilated patients, 7 had PE in CTPA. Among the 7 patients with bowel changes, 4 had PE in CTPA, indicating a significant association with PE. The observed bowel changes were attributed to intravascular thrombosis.

Conclusion. Based on our findings, individuals with COVID-19 often develop pulmonary emboli and bowel changes. Multivariate analyses revealed a connection between invasive mechanical ventilation and PE. Our results suggest that patients with severe clinical manifestations of COVID-19 may also have concurrent acute PE. Thus, for these patients, utilizing contrast-enhanced CT scans instead of standard non-contrast CT scans may aid in treatment decision-making.

Key words: COVID-19, coronavirus, severe acute respiratory illness, pulmonary embolism, gastrointestinal

BACKGROUND

The COVID-19 virus, also known as coronavirus 19, was initially identified in 2019 in the Wuhan province of China. Beginning as a common respiratory ailment, it swiftly spread worldwide, culminating in a pandemic. The COVID-19 pandemic, caused by the SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) virus, was officially declared a pandemic by the World Health Organization (WHO) in March 2020 [1].

The index case first appeared in Wuhan before the end of 2019. Its symptoms are similar to those of an upper respiratory tract infection or common cold but may also involve the lower respiratory tract. While many patients experience mild symptoms and recover without medical intervention, others develop severe illness necessitating intensive medical care. The virus primarily spreads via aerosol transmission and surface contact, inhalation of aerosols, and close interpersonal contact, occasionally transferring through direct contact with the eyes, nose, and mouth.

It is theorized that viral dissemination beyond the respiratory system during the second week of illness, coinciding with clinical deterioration, contributes to hypercoagulability and heightened immune-mediated injury. Researchers have suggested that pulmonary embolism (PE) may exacerbate cases of viral pneumonia, further compromising patient outcomes.

Indoor environments with poor ventilation and crowded conditions facilitate prolonged suspension of viral particles in the atmosphere, increasing transmission risk [2]. Individuals can become infected by inadvertently touching their eyes, nose, or mouth after contact with contaminated droplets.

Patients with COVID-19 infection primarily develop respiratory tract infections, with severe cases progressing to respiratory failure and multi-organ dysfunction. Severe disease-induced inflammation can disrupt coagulation homeostasis, with nearly 20% of COVID-19 patients exhibiting severe coagulation abnormalities, often manifesting as a hypercoagulable state [3]. Elevated plasma D-dimer levels upon admission have been correlated with higher mortality rates in COVID-19 patients [4].

Beyond coagulation abnormalities, both venous and arterial thrombosis have been linked to COVID-19 infection, particularly among critically ill patients [5]. Multiple studies have highlighted a heightened risk of PE in COVID-19 patients, primarily affecting segmental arteries. The early detection of PE is crucial for appropriate management and improved patient outcomes, particularly given the variability in recent research findings and consideration of other PE risk factors.

Furthermore, studies have documented disrupted coagulation function in COVID-19 patients compared to healthy individuals, with elevated D-dimer levels serving as a predictor of in-hospital mortality [6,7]. Radiological investigations have mainly centered on specific abnormalities visible on chest CT scans related to COVID-19, such as ground-glass opacities (GGOs) and consolidation, frequently appearing in both lung fields [8].

Recent studies highlight the link between inflammation triggered by COVID-19,

low oxygen levels, abnormal blood clotting, and thromboembolic issues, stressing the importance of preventive actions to avoid venous thromboembolism in COVID-19 patients receiving hospital care.

AIM

The study aims to assess radiological pulmonary vascular changes, specifically PE, in patients admitted with clinical signs and symptoms of COVID-19. Additionally, it seeks to evaluate radiological bowel and gastrointestinal changes in the same patient population. Furthermore, the correlation between the severity of pulmonary disease and the occurrence of PE will be examined. This research intends to shed light on the complex interplay between COVID-19 infection, its associated radiological manifestations in the pulmonary and gastrointestinal systems, and their potential implications for disease severity and management.

METHODS

The study design adopted for this investigation is a prospective cross-sectional study. The research was conducted over a duration of one year following approval from the ethical committee, spanning from September 2020 to August 2021. The sample size was determined utilizing the formula n = Z x Z x p x q/d x d, where n represents the sample size, Z denotes the statistically significant constant for a 95% confidence interval, p signifies the incidence of COVID-19 in patients with acute PE requiring mechanical ventilation from previous studies, q represents the complement of p, and d indicates the relative precision. After substitution of these values into the formula, the calculated sample size was determined to be 100 participants. This figure was adjusted to account for a 10% non-response rate, ensuring the robustness of the study's sample size.

The study population comprised 100 individuals that tested RT-PCR positive for COVID-19 and exhibited clinical signs and symptoms indicative of PE such as chest pain, shortness of breath, rapid heartbeat, cough, and in severe cases, cyanosis or low oxygen levels. These patients were referred to our department for CT scan evaluation.

Inclusion criteria encompassed individuals aged 18 years and above, confirmed RT-PCR positive for COVID-19, with plain CT chest studies revealing features consistent with PE such as peripheral wedge-shaped or segmental consolidations, and the presence of pleural effusions or infarcts. Additionally, patients demonstrating clinical manifestations of PE and those experiencing severe acute respiratory illness were included.

Conversely, exclusion criteria involved individuals below the age of 18, patients with diabetes, pregnant females, individuals with a known contrast allergy, and those with deranged renal function tests.

The study employed several tools for data collection, including written and informed consent from participants and a 128 multidetector CT scan machine (GE-Optima) for imaging purposes. Data collected encompassed the date of RT-PCR diagnosis, demographic information, and clinical data obtained within 72 hours of imaging. Furthermore, imaging data suggestive of PE and other pertinent features were also recorded.

Medical procedure description (Imaging Protocol)

CT pulmonary angiography (CTPA) was conducted with breath holding, utilizing 70–100 mL of iohexol (Omnipaque 300; GE Healthcare) as contrast agent. Bolus timing to achieve peak contrast enhancement (measured in Hounsfield Units) in the pulmonary artery was determined using Smart Prep (GE Healthcare) sampling at the mid superior vena cava. Data were reconstructed in axial view with a thickness of 1.25 mm, as well as 8-mm maximum intensity projection (MIP), and in coronal and sagittal planes at a section thickness of 1.25 mm, with 5-mm maximum

intensity projections (MIP). The images were analyzed using an OSIRIX workstation.

CTPA and abdominal CT image interpretation was done by a radiologist with an experience of 5 years in cross sectional imaging. The radiologist was aware of the clinical details of the patient. Using the OSIRIX workstation, multiplanar reformation (MPR) and MIP were used whenever needed.

Ethical review

a) Ethical Committee approved the study, GSMCH/IEC/29122020/005, c) 29/12/2020, and d) Government Stanley Medical College and Hospital – Institutional Ethics Committee

Statistical analysis

The gathered data underwent analysis using IBM SPSS Statistics for Windows, Version 26.0. Descriptive statistics, including frequency analysis for categorical variables and mean with standard deviation (SD) for continuous variables, were employed to characterize the data. A significance level of less than 0.05 was utilized across all statistical analyses.

RESULTS

The study presents a comprehensive analysis of various factors associated with PE in COVID-19 patients, drawing on data collected from a sample size of 100 individuals. The age distribution within the study population ranged from 17 to 85 years, with a mean age of 50 years and a standard deviation of 16.7 years. Notably, the majority of cases fell within the age groups of 41-50 years (25%) and >60 years (27%). Gender distribution revealed a higher proportion of male cases (61%) compared to females (39%).

Regarding comorbidities, 15% of patients had cardiovascular conditions, 7% had chronic respiratory insufficiency, and 5% had malignancies (Table 1). Plain CT scans indicated PE features in 3% of cases, while clinical symptoms suggestive of PE were observed in 6% of patients. Additionally, 24% of individuals exhibited clinical features of severe acute respiratory illness (SARI).

Further analysis involved pulmonary angiograms, revealing PE in 11% of cases. Notably, 10% of patients required invasive ventilation. The timing of pulmonary angiograms varied, with the majority (45%) conducted between 7-9 days of illness onset.

Statistical analyses were performed to evaluate the correlation between different factors and the occurrence of PE. These comparisons revealed no significant correlation between age (p=0.272) or gender (p=0.263) and PE. However, patients exhibiting clinical features of PE showed a significant association with PE detected via CTPA (p=0.001) (Table 2). Similarly, patients with signs of PE on plain CT scans exhibited a strong association with PE confirmed by CTPA (p=0.00001) (Table 3).

Moreover, patients with clinical features of SARI were significantly associated with PE (p=0.003) (Table 4). Furthermore, bowel changes observed in abdominal CT scans were significantly associated with PE (p=0.000054) (Table 5), as were patients requiring mechanical ventilation (p=0.00001) (Table 6).

Few illustrative cases showing pulmonary vascular changes and bowel changes in COVID-19 positive patients are shown in (Figures 1-3)

Overall, the study underscores the importance of considering clinical and radiological indicators in diagnosing PE in COVID-19 patients, particularly emphasizing the significance of symptoms such as respiratory distress and bowel changes, alongside imaging modalities like plain CT and CTPA.

DISCUSSION

In our study, 100 COVID-19 positive patients underwent CTPA. Among these cases, 11 patients exhibited pulmonary thromboembolism, while 7 patients showed

significant bowel changes. Our findings indicate a positive correlation between the prevalence of PE in COVID-19 patients. Pulmonary embolus was typically diagnosed at a mean of 11 days from the onset of disease. Danzi GB et al. demonstrated that severe COVID-19 is associated with PE [9]. In our study, out of 24 SARI patients, 7 showed PE in CTPA. Chi G, et al., and Grillet F, et al., revealed that COVID-19 patients with PE are more likely to require mechanical ventilation compared to those without PE [10,11]. In our study, out of 10 mechanically ventilated patients, 7 had PE in CTPA.

We noted that the extent of the lesion showed no correlation with PE. We recognize the preliminary nature of these findings within the South Indian population, considering the retrospective design and the limited sample size. Several crucial clinical indicators, such as D-dimer levels, were absent, which might elucidate the association of PE in COVID-19 patients. Nonetheless, our study indicates that severe COVID-19 patients could develop PE, underscoring the potential utility of CTPA in guiding treatment decisions in such cases.

Abdelmohsen, et al. showed that there are significant bowel changes in COVID-19 patients [12]. In our study, significant bowel changes (observed in 7 patients) manifested as bowel wall thickening, mesenteric ischemia, and omental infarction. Out of these 7 patients, 4 had PE in CTPA, indicating a significant association with PE. The observed bowel changes may also be attributed to intravascular thrombosis. Potential reasons for the gastrointestinal changes in individuals with COVID-19 encompass direct viral invasion, thrombosis in small blood vessels, or non-occlusive mesenteric ischemia.

Research limitations

The study possesses several notable limitations that warrant acknowledgment. Firstly, due to its cross-sectional design, the investigation lacks the capacity to analyze patient follow-up and survival data, which could provide valuable insights into the long-term outcomes associated with PE in COVID-19 patients. Secondly, the relatively small sample size raises concerns regarding the generalizability of the findings to the broader population. Thirdly, the absence of biochemical investigations, such as D-dimer levels, represents a significant limitation as these markers could provide crucial insights into the correlation between D-dimer levels and PE formation. Furthermore, the presence of confounding factors, such as malignancy, in some cases presents challenges in discerning whether PE is directly attributable to COVID-19 or other underlying conditions. Moreover, the retrospective nature of data collection introduces inherent biases and limitations in controlling for various factors that may influence the outcomes under investigation. These limitations underscore the need for caution in interpreting the study findings and emphasize the importance of conducting further research with larger sample sizes and prospective designs to validate and expand upon the observed associations.

CONCLUSION

The typical assessment of COVID-19 and its extent often involves non-contrast chest CT, as per current guidelines. Previous findings have indicated a correlation between coagulopathy and COVID-19 infection. Moreover, these patients frequently present with risk factors for PE, such as mechanical ventilation and admission to an intensive care unit. To evaluate lung parenchyma and potential causes of respiratory distress comprehensively, we advocate for contrast-enhanced CT scans in COVID-19 patients exhibiting severe clinical symptoms.

Our findings reveal that individuals with COVID-19 commonly experience pulmonary emboli and bowel changes. Multivariate analyses identified a connection between invasive mechanical ventilation and PE. Unfortunately, crucial clinical indicators like D-dimer levels were unavailable, limiting our ability to explain or correlate with PE. Nevertheless, our results suggest that patients with severe COVID-19 symptoms may have an associated acute PE. Consequently, for these patients, the utilization of contrast-enhanced CT scans, as opposed to

standard non-contrast CT, could aid in the early detection of vascular changes and facilitate treatment planning.

ADDITIONAL INFORMATION

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Authors involvement.

HS: study design, collection of data, data analysis, and writing of the manuscript.

AF: writing of the manuscript, sourcing and editing of clinical images, critical review, and investigation results.

VR: sourcing and editing clinical images, investigation results, critical review and revision.

All authors have critically reviewed and approved the final draft and are responsible for the manuscript's content and similarity index.

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TABLES

TABLE 1 – COMPARISON OF COMORBIDITIES OF PATIENTS WITH CT PULMONARY ANGIOGRAPHY (CTPA) SHOWING PULMONARY EMBOLISM (PE)

Comorbidities	**CTPA showing PE**		**Total**
	Yes	**No**	
	N (%)	**N (%)**	
Cardiovascular	4	11	15
Chronic respiratory insufficiency	2	5	7
Malignancy	1	4	5
Absent	4	69	73
Total	11	89	100

TABLE 2 – COMPARISON OF PATIENTS SHOWING CLINICAL FEATURES OF PE WITH PE DETECTED AT CTPA BY CHI SQUARE TEST WERE x^2=9.9, P=<0.05 WHICH SHOWS HIGH STATISTICAL SIGNIFICANCE

Clinical Features of PE	CTPA showing PE		Total	P value
	Yes	No		
	N (%)	N (%)		
Yes	3 (27)	3 (3)	6	0.001*
No	8 (73)	86 (97)	94	
Total	11	89	100	

*P value < 0.05 significant using Chi Square Test

TABLE 3 – COMPARISON OF PATIENTS SHOWING SIGNS OF PE IN PLAIN CT WITH PE DETECTED AT CTPA BY CHI SQUARE TEST WERE X^2=24.91, P=<0.05 WHICH SHOWS HIGH STATISTICAL SIGNIFICANCE

PE in plain CT	CTPA showing PE		Total	P value
	Yes	No		
	N (%)	N (%)		
Yes	3 (27)	0	3	0.00001*
No	8 (73)	89 (100)	97	
Total	11	89	100	

*P value < 0.05 significant using Chi Square Test

TABLE 4 – COMPARISON OF PATIENTS SHOWING SEVERE ACUTE RESPIRATORY ILLNESS (SARI) WITH PE DETECTED AT CTPA BY CHI SQUARE TEST WERE x^2=9.96, P=<0.05 WHICH SHOWS HIGH STATISTICAL SIGNIFICANCE

SARI	CTPA showing PE		Total	P value
	Yes	No		
	N (%)	N (%)		
Yes	7 (29)	17 (71)	24	0.003*
No	4 (5)	72 (95)	76	
Total	11	89	100	

*P value < 0.05 significant using Chi Square Test

TABLE 5 – COMPARISON OF CT ABDOMEN SHOWING BOWEL CHANGES WITH PE DETECTED AT CTPA BY CHI SQUARE TEST WERE x^2=16.30, P=<0.05 WHICH SHOWS HIGH STATISTICAL SIGNIFICANCE

Bowel changes in CT abdomen	CTPA showing PE		Total	P value
	Yes	No		
	N (%)	N (%)		
Yes	4 (57)	3 (43)	7	0.000054*
No	7 (8)	86 (92)	93	
Total	11	89	100	

*P value < 0.05 significant using Chi Square Test

TABLE 6 – COMPARISON OF COVID-19 ON MECHANICAL VENTILATION WITH PE DETECTED AT CTPA BY CHI SQUARE TEST WERE x^2=39.47, P=<0.05 WHICH SHOWS HIGH STATISTICAL SIGNIFICANCE

COVID-19 patients on Mechanical Ventilation	CTPA showing PE		Total	P value
	Yes	No		
	N (%)	N (%)		
Yes	7 (64)	3 (3)	10	0.00001*
No	4 (36)	86 (97)	90	
Total	11	89	100	

*P value < 0.05 significant using Chi Square Test

FIGURES

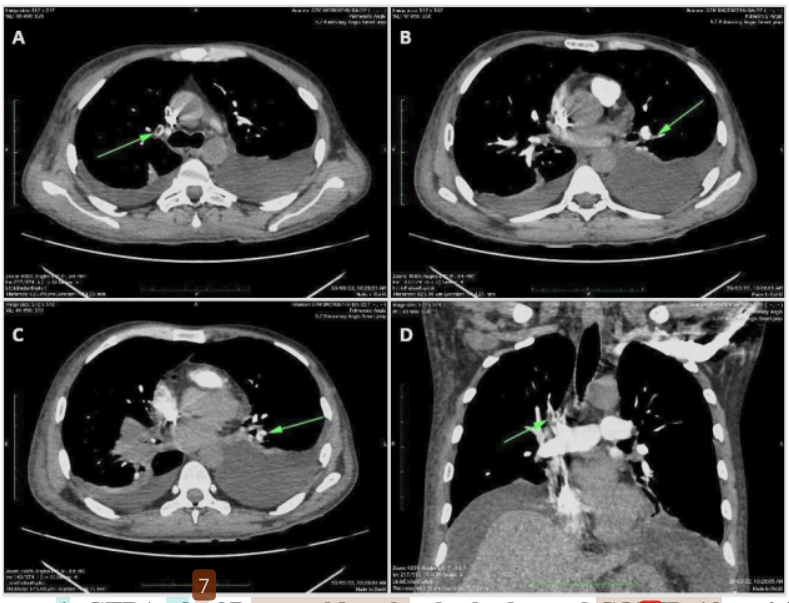

Figure 1: CTPA of a 27-year-old male who had tested COVID-19 positive showing bilateral pleural effusions and A) thrombus in the right upper lobe pulmonary artery just proximal to segmental branches B) thrombus in the left lower lobe lateral segmental artery C) thrombus in the left lower lobe pulmonary artery before dividing into branches D) thrombus in the right upper lobe pulmonary artery just proximal to segmental branches.

Figure 2: CTPA of a 33-year-old male who had tested COVID-19 positive showing A) thrombus in the left lower lobe posterior segment B) a soft tissue dense lesion in the left lung invading the adjacent rib and a lytic lesion noted in the thoracic vertebra

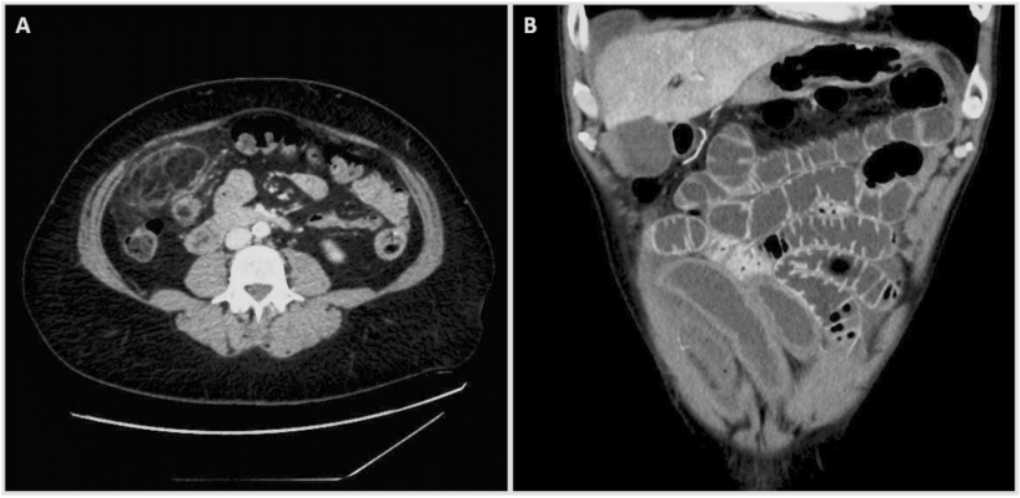

Figure 3: Contrast enhanced CT abdomen images of a 34-year-old male who had tested COVID-19 positive showing A) omental fat stranding in the right side of the lower abdomen consistent with omental infarction B) mural thickening in the distal ileum with hypoenhancement compared to the adjacent bowel.

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