Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
The prevalence of pulmonary embolism among COVID-19 patients underwent CT pulmonary angiography

Samih Kajoak a, Hamid Osman a,*, Hanan Elnour a, Amin Elzaki a, Ahmad Joman Alghamdi a, Mona Elhaj b, Ahmad Alotaibi a, Khaled Alboqami b, Fahad Alturaiki b, Ali Alsulaimani a, Kholoud Alsulimany b, Mayeen Udinn Khandaker c, Sultan Alamri a, Yasser Alzamil a

a Department of Radiological Sciences, College of Applied Medical Sciences, Taif University, P.O. Box: 11099, 21944, Taif, Saudi Arabia
b King Faisal Medical Complex, Taif, Saudi Arabia
c Centre for Applied Physics and Radiation Technologies, School of Engineering and Technology, Sunway University, Bandar Sunway, 47500, Malaysia

* Corresponding author.

1. Introduction

Coronavirus disease 2019 (COVID-19) is a highly contagious disease caused by the SARS-CoV-2 virus that affects the respiratory system of the human body. Soon after the detection of the first case in Wuhan, China on December 31, 2019, it has been spread quickly around the world and became a global pandemic (About the virus, 2022). On March 2, 2020, in Saudi Arabia, the first case was announced by the ministry of health, and as of July 31, 2022, the total number of confirmed cases was 810 K with about 9 K deaths.

The statistics show that Covid-19 patients had mild symptoms including fever, cough, fatigue, loss of taste/smell, and rhinorrhea (Lovato et al., 2020). In addition, some patients may develop respiratory failure. Although the underlying reason for respiratory deterioration including fever, cough, fatigue, loss of taste/smell, and rhinorrhea (Lovato et al., 2020). In addition, some patients may develop respiratory failure. Although the underlying reason for respiratory deterioration...
varies from person to person, the development of acute respiratory distress syndrome (ARDS), progression of viral pneumonia, and pulmonary emboli are considered major contributing factors. The diagnosis of ARDS, pneumonia and PE in COVID-19 patients is challenging with significant therapeutic implications. Consequently, several international guidelines recommend the use of low-dose non-enhanced CT (LDCT) for assessing the severity of COVID-19 pneumonia (Rubin et al., 2020; Vogel-Clausen et al., 2020). Therefore, PE can be ruled out as a cause of sudden respiratory deterioration. Moreover, the patients who suffer from severe pneumonia, show deficiency in some signs and symptoms that are needed to initiate diagnostic evaluation for PE. This kind of COVID-19 patients shows elevated levels of d-dimer (Yu et al., 2020).

Pulmonary embolism occurs when a blood clot (thrombus) causes a blockage in the main pulmonary artery or its bifurcation, this clot arises from deep leg veins in 95% of cases. PE affects about 300,000–600,000 humans every year and an estimated 100,000 deaths per year in the USA (Beckman et al., 2010), due to the inconsistency of signs and symptoms, resulting in the misdiagnosis by doctors. COVID-19 infections usually cause the coagulation system to be activated. This is known as COVID-19 hypercoagulability, and it results in many complications to the relevant COVID-19 patients followed by high mortality and morbidity rates (Connors & Levy, 2020).

Computed tomography pulmonary angiography (CTPA) provides many advantages over other modalities in diagnosing PE because it is fast, noninvasive, widely available, and includes direct visualization of the embolus cross-sections in multiple planes. Therefore, it is considered the best modality to diagnose patients with PE. Normal pulmonary vessels appear as a bright white when the contrast agent is injected unlike PE appears as a contrast filling defect (Albert et al., 2008; Hamid, 2021). There is a lack of publication from our community according to literature available for authors, regarding the prevalence of PE, consequently the present study aims to investigate the prevalence of PE among COVID-19 patients who have undergone CTPA examinations and the factors associated with the severity of PE.

2. Materials and methods

This is a retrospective cross-sectional study to investigate the prevalence of PE in COVID-19 patients who have been examined by CT pulmonary angiography and the factors associated with the severity of PE. The study was conducted at King Faisal Medical Complex in Taif, from June 2020 to June 2021. The inclusion criteria of COVID-19 patients include males and females of age greater than 21 years. All data were collected from the picture archiving and communication system (PACS) for all patients who were tested positive for COVID-19 and underwent CT pulmonary angiography.

The search term “pulmonary embolism” was used to identify CT pulmonary angiography examinations performed from December 2020 to September 2021. The electronic medical record for the patients was reviewed to identify those who were confirmed to have COVID-19 infection by reverse transcription polymerase chain reaction (r-PCR) testing of nasopharyngeal or oropharyngeal swab samples. Only the patients who tested positive for COVID-19 with r-PCR were included in the study sample. Note that the King Faisal Medical Complex is the only designated center for the treatment of COVID-19 patients in Taif city and it is equipped with two CT machines dedicated to diagnosing COVID-19 patients only during the pandemic. The CTPA examination is performed as a protocol for any patient admitted to the hospital who had tested COVID-19 positive. It has been found that most patients are admitted to the hospital in the early stage of the COVID-19 symptom. The study was ethically approved by the administration of research and studies in the directorate of health affairs-Taif city, Saudi Arabia.

CT Protocol: All examinations protocol were performed at the aforementioned King Faisal Medical Complex. Either 64 or 256 slices were obtained by computed tomography scanners (Siemens/GE) during the inspiration phase. The patient was supine and arms above the head and injected with 40–70 ml omnipaque (iohexol injection) contrast media (according to the patient’s weight) together with 20 ml of normal saline, the flow rate was 5 mL/s. The scan direction was caudocranial from the diaphragm to apices (slice thickness 0.6 mm).

3. Statistical analysis

The results are summarized as mean ± SD in the relevant tables shown in later sections. Data were analyzed by applying the standard Statistical Package for the Social Sciences (SPSS) version 23. The P-value of <0.001 was considered significant.

4. Results

In this study, a total of 445 participants were included. The mean age of respondents was 57.3 ± 15.8 years (range 21–112), most of them were males (64.5%) and 158 (35.5%) were females. Present results revealed that BI ground-glass opacity (BI GGO) was the most common reported CT finding among the participants (76.6%) followed by normal CT finding (11.9%), then pleural effusion shown by (11%) of respondents. Moreover, the CT findings demonstrated that only 6.5%, 5.2%, and 3.4% of participants showed bilateral pleural effusion, multifocal pneumonia, and ground-glass opacities (GGO) respectively (Table 1).

4.1. The prevalence of PE in COVID-19 patients experienced CTPA examinations

This study found that the prevalence of pulmonary embolism at CT pulmonary angiography was 8.1% among the patients with COVID-19 symptoms who were admitted to the King Faisal Medical Complex (KFMC) in Taif city of Saudi Arabia (see Fig. 1).

Pulmonary Embolism sites: Present results showed that bilateral segmental (16.7%) and bilateral subsegmental (16.7%) were equally the most common sites for Pulmonary Embolism among the respondents followed by bilateral segmental and subsegmental (13.9%), left lower segmental (8.3%), left lower subsegmental (8.3%), and right segmental (8.3%). On the other side, left segmental and left subsegmental were reported at (11%) collectively (Table 2) (Figs. 2-5).

Symptoms among the study population: Present results showed that shortness of breath (SOB) is the most common documented symptom among the respondents (66.5%). Almost the same proportion of participants (65.4%) experienced chest pain followed by the symptoms of loss of taste or smell (63.1%). Additionally, we found that cough,
fever and headache were reported by nearly forty percent (40%) of the participants. Only 15.5% of respondents suffered from sore throats (Fig. 6). The prevalence of PE in COVID-19 patients in different studies is shown in Fig. 7.

Laboratory investigations: Based on the laboratory investigations, it has been found that the average level of D-dimer was 2.3 ± 3.2 μg/mL (range 0.2–18.6), the average level of Lactate dehydrogenase was 380.9 ± 177.4 U/L (range 148–1192) and the average level of Cardiac Troponin was 32 ± 107.6 pg/mL (range 3–801.8).

4.2. Association between demographic and clinical characteristics with pulmonary embolism

Present results have shown a non-significant association between demographic variables (age and gender) and pulmonary embolism among the study population. However, there was a positive significant association between pulmonary embolism and shortness of breath, chest pain and loss of taste or smell (P values = < 0.001, <0.001 and 0.001 respectively). Based on the laboratory test results, the D-dimer and Cardiac troponin levels revealed a significant association with pulmonary embolism (P values = < 0.001 and 0.037 respectively) as shown in Table 3. The pulmonary Embolism site compared to other studies is shown in Table 4.

5. Discussion

This is a retrospective cross-sectional study that assessed the prevalence of pulmonary embolism in patients who tested positive for coronavirus disease and were examined by CT pulmonary angiography at King Faisal Medical Complex (KFMC) in Taif city of Saudi Arabia. COVID-19 may predispose patients to thrombotic complications as a result of excessive inflammation, platelet activation, endothelial dysfunction, and stasis (Bikdeli et al., 2020). The impact of thrombotic complications is increasingly recognized as an important component of this disease, and a subset of patients who develop severe respiratory distress syndrome, sepsis, septic shock, and pulmonary embolism
requires more likely mechanical ventilation and critical care unit for recovery than the patients who do not have a pulmonary embolism (Awulachew et al., 2020).

A review of the literature shows that several studies from around the world have assessed the prevalence of PE in COVID19 patients only recently, beginning with a single case and small-series reports (Danzi et al., 2020; Fabre et al., 2020; Rotzinger et al., 2020; Ullah et al., 2020; Xie et al., 2020). In the current study, we found that the prevalence of PE at CT Pulmonary Angiography was 8.1% among patients with COVID-19. This prevalence was lower than in some other studies conducted in Saudi Arabia, with rates between 12% and 32% (Abohamr et al., 2021; Badr et al., 2021; Bukhari et al., 2021). Other studies in Italy, New York, Spain, and the UK revealed a very high prevalence of PE among COVID-19 patients, 40%, 37.1%, 50%, and 38% respectively (Alonso-Fernández et al., 2020; Kaminetzky et al., 2020; Masselli et al., 2021; Ooi et al., 2020). However, earlier studies in Spain and UK demonstrated a lower rate of PE prevalence 6.4% and 5.4% respectively among COVID 19 patients (Mestre-Gómez et al., 2020; Whyte et al., 2020).

![Fig. 4. CTPA of 37 years old female with Covid-19 demonstrates PE in the left lower and right lower segmental pulmonary artery (red arrow).](image1)

![Fig. 5. CTPA of 69 years old male with Covid-19 demonstrates PE in the bilateral lower segmental branches (red arrow) and Ground Glass Opacification (yellow arrow).](image2)

![Fig. 6. Symptoms among the study population (n = 445).](image3)

![Fig. 7. The prevalence of pulmonary embolism in COVID-19 patients in different studies.](image4)

![Table 3 Association between demographic and clinical characteristics with PE.](table)

| Variable                      | APE N = 36 | Non-PE N = 409 | P value  |
|-------------------------------|------------|----------------|----------|
| Demographic data:             |            |                |          |
| Age (years) (mean ± SD)       | 56.1 (16.3) | 57.4 (15.7)    | 0.633    |
| Gender, n (%) Male            | 22 (61.1%) | 265 (64.8%)    | 0.658    |
| Female                        | 14 (38.9%) | 144 (35.2%)    |          |
| Department ICU                | 34 (94.4%) | 401 (98%)      | 0.162    |
| Emergency                     | 2 (5.6%)   | 8 (2%)         |          |
| Clinical presentation: n (%)  |            |                |          |
| Fever                         | 20 (55.6%) | 161 (39.4%)    | 0.058    |
| SOB                           | 35 (97.2%) | 263 (63.8%)    | < 0.001  |
| Sore throat                   | 3 (8.3%)   | 66 (16.1%)     | 0.215    |
| Chest pain                    | 35 (97.2%) | 256 (62.6%)    | < 0.001  |
| Cough                         | 20 (55.6%) | 168 (41.1%)    | 0.092    |
| Loss of taste or smell        | 32 (88.9%) | 249 (60.9%)    | 0.001    |
| Headache                      | 18 (50%)   | 160 (39.1%)    | 0.201    |
| Not mentioned                 | 0 (0)      | 14 (3.4%)      | 0.259    |

| Laboratory tests: median (in quartile range 25% - 75%) | |
|--------------------------------------------------------|-----------------|
| D-dimer test ug/ml                                     | 3.5 (1.1–7.1)   | 1.0 (0.7–1.9) | < 0.001 |
| Lactate Dehydrogenase U/L                              | 342 (267.5–420) | 385.5 (278–522) | 0.637   |
| Cardiac troponin pg/ml                                  | 13.2 (8.5–52.5) | 8.6 (6.1–12.2) | 0.037   |
2020, pp. 95–99) (see Fig. 7). This may indicate that the differences between these studies are due to variations in the clinical condition of the sample population, which is explained in a systemic review from the Netherlands which concluded that the frequency of PE in patients with COVID-19 is highest in the ICU, followed by general wards and the emergency department (Kwee et al., 2021, pp. 1–19). It has been found that the results of the systemic review are similar to our results, most PE patients 34 (94.4%) were from the intensive care unit and 2 (5.6%) were from the emergency department. Moreover, the effect of vaccines should be considered while calculating the reduction of prevalence and incidence of PE. It is assumed that some of the above-mentioned studies were conducted before the development and successful administration of COVID-19 vaccines. In addition, the observed frequency of PE also depends on the selection criteria for CT Pulmonary Angiography.

The current study revealed that Bilateral segmental and Bilateral subsegmental were the most common sites for PE in the current participants. A case-control study in Saudi Arabia has reported similar results to ours, namely that unilateral acute PE was seen in 3/11 cases, three cases of PE at the lobar level, three cases at the segmental level, and five cases at the lobar, segmental, and subsegmental levels (Darwish et al., 2021, pp. 1–5). Another study in Spain supported this finding (Alonso-Fernandez et al., 2020) (Table 4).

Several studies have reported that D-dimer levels are significantly associated with pulmonary embolism in COVID-19 patients (Alonso-Fernandez et al., 2020; Darwish et al., 2021, pp. 1–5; Masselli et al., 2021). The D-dimer level appears to be an important parameter in the management of COVID-19 patients, allowing both the severity of the disease (Zhou et al., 2020) and the suspicion of acute pulmonary embolism (APE). Given that an increase in D-dimer levels has been linked to COVID-19, it would be interesting to see if there is a cut-off D-dimer level at which CTPA could be recommended to look for APE in COVID-19 patients based on large-scale studies (Leonard-Lorant et al., 2020). Moreover, we found other associated factors with PE such as shortness of breath, chest pain, loss of taste or smell, and cardiac troponin level. Also, another study in Saudi Arabia (Abohamr et al., 2021) showed a significant association between PE in COVID-19 patients and cardiac troponin levels, which is in agreement with the present study. This indicates that more studies are needed to have a better understanding of the pathophysiology of PE among COVID-19 patients.

6. Conclusion

This study shows that the prevalence of pulmonary embolism among COVID-19 patients diagnosed by CT Pulmonary Angiography at King Faisal Medical Complex in Taif city of Saudi Arabia is relatively low (8.1%) and most of the patients were from the ICU department. Preventive measures should be considered for hospitalized patients who have shortness of breath, chest pain, loss of taste or smell, and elevated D-dimer and cardiac troponin levels. Early detection and treatment of COVID-19 patients with PE and APE complications are critically needed for lowering the mortality rate. More studies are needed to assess the risk factors and thrombosis mechanisms associated with the COVID-19 symptoms.

7. Limitations

Due to the retrospective study design, it was not possible to establish a causal relationship between COVID-19 and pulmonary embolism. Furthermore, the present study utilized the data that was obtained only from King Faisal Medical Complex in Taif, which is recognized as the COVID-19 Center in Taif city of Saudi Arabia. Data obtained from several designated hospitals may provide more accurate results by removing any possible bias with many known/unknown local/regional factors.

Acknowledgements

The authors deeply acknowledge Taif University for supporting this research through Taif University Researchers Supporting project number (TURSP-2020/287), Taif University, Taif, Saudi Arabia.

References

Abohamr, S. I., Aldossari, M. A., Amer, H. A., Saadeddin, H. M., Abdelhamid, S. W., Bhat, F. A., & Abdul Aziz Elsheikh, E. (2021). The incidence of acute pulmonary embolism with COVID-19 pneumonia in Saudi Arabia: A retrospective single-center study. Journal of the Heart Association, 3(2), 128–134. https://doi.org/10.37616/2212-5043.1253
Albert, R. K., Spro, S. G., & Jett, J. R. (2008). Clinical respiratory medicine. Clinical Respiratory Medicine, 61, 763–781.
Alonso-Fernandez, A., Toledo-Pons, N., Cosio, B. G., Millan, A., Calvo, N., Ramon, L. de Mendoza, S. H., Morell-Garcia, D., Basca-Roselllo, J. M., Núñez, B., Pons, J., Palmer, J. A., Martin, L., Periandras, M., Pou, J. A., Saulela, J., & Sala-Llinas, E. (2020). Prevalence of pulmonary embolism in patients with COVID-19 pneumonia and high D-dimer values: A prospective study. PLoS One, 15(8), Article e0238216. https://doi.org/10.1371/journal.pone.0238216
Awulachew, E., Diriba, K., Anja, A., Getu, E., & Belalyneh, F. (2020). Computed tomography (CT) imaging features of patients with COVID-19: Systematic review and meta-analysis. Radiology Research and Practice, 1–8. https://doi.org/10.1155/2020/1025056, 2020.
Badr, O. I., Alwafi, I., Elrefaey, W. A., Naser, A. Y., Shabrawiwi, M., Alsaifi, Z., & Alsaehe, F. M. (2021). Incidence and outcomes of pulmonary embolism among hospitalized COVID-19 patients. International Journal of Environmental Research and Public Health, 18(14), 7645. https://doi.org/10.3390/ijerph18147645
Beckman, M., Hooper, W., Critchley, S., & Ortel, T. (2010). Venous thromboembolism. American Journal of Preventive Medicine, 38(4), 5495–5501. https://doi.org/10.1016/j.amepre.2009.12.017
Bikdeli, B., Madhavan, M.V., Jimenez, D., Chuich, T., Dreyfus, I., Driggan, E., et al. (2020). COVID-19 and thrombotic or thromboembolic disease: Implications for prevention, antithrombotic therapy, and follow-up. Journal of the American College of Cardiology, 75(23), 2950–2973. https://doi.org/10.1016/j.jacc.2020.04.031
Bukhari, Z. M., Alqarni, S. M., Abboshodair, A. W., Alzahrani, A. S., Alzahrani, A., Alsaleh, H., Alsadah, F., Alostaib, A. M., & Alhobabi, M. (2021). COVID-19-related pulmonary embolism: Incidence, characteristics, and risk factors. Careus. https://doi.org/10.7759/careus.19738
Connors, J., & Levy, J. (2020). Thromboinflammation and the hypercoagulability of COVID-19. Journal of Thrombosis and Haemostasis, 18(7), 1559–1561. https://doi.org/10.1111/jth.14849
Danzi, G., Loffi, M., Galeazzi, G., & Gherbesi, E. (2020). Acute pulmonary embolism and COVID-19 pneumonia: A random association. European Heart Journal, 41(19). https://doi.org/10.1093/eurheartj/ehaa254, 1858–1858.
Darwish, H. S., Habash, M. Y., & Habash, W. Y. (2021). COVID-19 viral pneumonia complicated with acute pulmonary embolism: A descriptive study. Radiology Research and Practice. https://doi.org/10.1155/2021/6649086, 2021.
Fabel, O., Rebet, O., Carjaliu, I., Radutoiu, M., Gautier, L., & Hyst, I. (2020). Severe acute proximal pulmonary embolism and COVID-19: A word of caution. The Annals of Thoracic Surgery, 110(5), e409-e411. https://doi.org/10.1016/j.athoracsur.2020.04.005
Hamid, H. O. (2021). Role of computed tomography angiography in detecting pulmonary embolism and the prevalence of it. Medical Science, 25(109), 716–722.
Kaminetzky, M., Moore, W., Fanswala, K., Bahb, J. S., Kaminetzky, D., Horwitz, L. I., McGuinness, G., Knoll, A., & Ko, J. P. (2020). Pulmonary embolism on CTPA in COVID-19 patients. Radiology. Cardiothoracic Imaging. https://doi.org/10.1148/ rcm.2020200506 [online] 5(4).
Kwee, R. M., Adams, H. J. A., & Kwee, T. C. (2021). Pulmonary embolism in patients with COVID-19 and value of D-dimer assessment: A meta-analysis. European Radiology. https://doi.org/10.1007/s00330-021-08065-8 [online] pp.
Leonard-Lorant, I., Delabranche, X., Severac, F., Helms, J., Pauzet, C., Collange, O., Schneider, F., Labani, A., Bilbault, P., Moliere, S., Leyendecker, P., Roy, C., & Ohana, M. (2020). Acute pulmonary embolism in COVID-19 patients on CT angiography and relationship to D-dimer levels. Radiology, Article 201561. https://doi.org/10.1148/radiol.2020201561

Table 4

| Pulmonary Embolism Site compared to other studies. |
|-----------------------------------------------|
| Our Findings | Spain | Saudi Arabia |
| Bilateral | 50% | 60% | 72.7% |
| Segmental | 30.5% | 53% | 27.3% |
| Subsegmental | 13.9% | 7% | None |
| Unilateral (Segmental - Subsegmental) | 5.6% | None | None |
