Archives of Anesthesiology and Critical Care (In Press); x(x): xx-xx.

Available online at http://aacc.tums.ac.ir

Research Article

Assessment of D-Dimer and Ferritin as Predictive Biomarkers for Thromboembolic Events in Hospitalized COVID-19 Patients at Modares Hospital: A Retrospective Study

Sasan Tavana[1], Ali Dabbagh[2,3], Fatemeh Soltaninia[4]*

[1]*Department of Pulmonary Medicine, Clinical Research and Development Center, Shahid Modarres Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran.*

[2]*Department of Anesthesiology, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran.*

[3]*Anesthesiology Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.*

[4]*School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran.*

ARTICLE INFO

Article history:
Received 25 February 2025
Revised 16 March 2025
Accepted 29 March 2025

Keywords:
COVID-19;
Thromboembolism;
Prognosis;
D-dimer;
Ferritin

ABSTRACT

Background: The COVID-19 pandemic has been associated with a significant prevalence of thromboembolism. This study aimed to identify the predictive effect of D-dimer and ferritin on thromboembolism occurrences in hospitalized COVID-19 patients.

Methods: This retrospective study examined 304 patients with COVID-19, with a mean age of 62.33 ± 17 years, hospitalized at Modares Hospital from March 2020 to March 2021. The case group (PTE) comprised patients who experienced thrombosis complications during hospitalization (152 patients), while the control group (Non-PTE) consisted of patients who did not encounter thrombosis complications during their hospital stay (152 patients). Demographic data, clinical information, and laboratory findings were gathered and documented from patient records. The study examined the impact of D-dimer and ferritin as predictors of thromboembolism in patients.

Results: In this study, 100 patients died, with 75 (75%) of these fatalities occurring in the PTE group. The results indicated that PTE patients exhibited higher BMI (28.36 ± 1.87 vs. 27.76 ± 1.31 kg/cm², P<0.001), longer hospital stays (11.2 vs. 8.5 days, P=0.0009), increased ICU admissions (61.8 vs. 26.3%, P<0.001), higher smoking rates (21.9 vs. 4.8%, P<0.001), and greater prevalence of chronic lung disease (13.2 vs. 2.6%, P=0.001) compared to non-PTE patients. Analysis of the laboratory findings indicated a significant increase in lymphocyte count (P=0.034) and C-reactive protein (CRP) 3+ levels (P=0.04) in the PTE group compared to the non-PTE group. The D-dimer concentration in the PTE group was 4178.80 ± 1148.78 ng/ml, while in the non-PTE group it was 606.04 ± 656.86 ng/ml (1.03 OR, 95% CI=1.04-1.02, P<0.001). The ferritin level in the PTE group was recorded at 1639.33 ± 514.38, while in the Non-PTE group, a measurement of 420.48 ± 322.65 ng/ml was recorded (OR: 1.06, CI95%=1.07-1.04, P<0.001).

Conclusion: Elevated serum levels of ferritin and D-dimer in COVID-19 patients correlate with an increased risk of thromboembolism. Consequently, elevated concentrations of these parameters in hospitalized patients should serve as a warning to clinicians, necessitating careful attention and prompt treatment interventions.

The authors declare no conflicts of interest.

*Corresponding author.
E-mail address: azadehsoltaninia9@gmail.com

DOI:

Copyright © 2025 Tehran University of Medical Sciences. Published by Tehran University of Medical Sciences.

This work is licensed under a Creative Commons Attribution-NonCommercial 4.0 International license (https://creativecommons.org/licenses/by-nc/4.0/). Noncommercial uses of the work are permitted, provided the original work is properly cited.

Introduction

COVID-19 is an infectious disease caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). Initially, it was believed that COVID-19 primarily affects the lungs. Chest CT scans were primarily utilized to assess the lungs and served as a significant aid for clinicians [1]. Subsequent research has demonstrated that COVID-19 affects multiple organs. Consequently, researchers looked for a systemic parameter to assist clinicians in achieving a comprehensive understanding of all organs, not solely the lungs [2]. Inflammatory biomarkers were suggested as indicators that assisted clinicians in assessing systemic disease beyond the pulmonary system [3].

Inflammatory biomarkers in blood tests may assist clinicians in assessing hospitalized patients and predicting complications associated with COVID-19. Studies indicate that increased levels of inflammatory markers, specifically ferritin and D-dimer, in COVID-19 patients correlate with the severity of SARS-CoV-2 infection, the necessity for ICU admission, and in-hospital mortality [4-6]. Inflammatory biomarkers may contribute to the cytokine storm observed in COVID-19 patients, subsequently leading to lung injury. Lung injury results in hypoxia and acute respiratory distress syndrome (ARDS), which can lead to mortality. Cytokine storm also induces pulmonary thromboembolism, complicating the disease and increasing the risk of mortality [7].

D-dimer, while nonspecific, serves as a marker for the severity of COVID-19. Thus, it may provide data regarding both inflammation and pulmonary thromboembolism (PTE) in patients with COVID-19. This study evaluates the accuracy and power of ferritin and D-dimer in predicting mortality and pulmonary thromboembolism in hospitalized COVID-19 patients.

Methods

This study aimed to investigate the predictive role of D-dimer and ferritin on the occurrence of thromboembolism in COVID-19 patients hospitalized in 2019 at Modares Hospital. This research constituted a single-center retrospective analysis. Following the approval of the project by the Research Council and the Ethics Committee of Shahid Beheshti University of Medical Sciences, sampling and data extraction commenced in accordance with the established input criteria for the samples.

Selection and randomization

The study included patients with COVID-19 who had at least one positive PCR test and were indicated for hospitalization from March 2020 to March 2021. Exclusion criteria comprised patients with incomplete file information, those with a history of coagulopathy, and individuals who did not give informed consent for the inclusion of their data in research projects. A total of 152 patients with COVID-19 experiencing thromboembolic complications were selected as the case group, while 152 patients without thromboembolic complications were assigned to the control group, resulting in 304 COVID-19 patients within the specified time frame.

The control group was selected by randomly choosing each case from the population of COVID-19 patients under investigation over a one-year period, maintaining a ratio of 1 control to 1 case in accordance with the calculated sample size.

Following the selection of each case, a witness was randomly chosen from the patient list acquired from the medical records unit, based on the date and ward of hospitalization. The control group was selected through the allocation of 150 random numbers in an Excel file, corresponding to a list of COVID-19 patients without thrombosis over a one-year period.

Demographic and clinical information was obtained from clinical records, while laboratory values, including inflammatory factors and cardiac enzymes, were extracted from reports during hospitalization, specifically the first values recorded within the initial 24 hours of admission.

Data analysis method

The normal distribution of quantitative variables was initially assessed using a histogram. Quantitative variables were reported using mean and standard deviation (SD), while grouped variables were described using frequency and percentage. The parametric t-test was employed to compare the averages of quantitative variables between two groups, while the non-parametric Mann-Whitney U test was utilized when the quantitative variables did not meet a normal distribution.

Appropriate statistical tests, such as the Chi-square test or Fisher's exact test, have been employed to assess the differences in the distribution of the grouped variables. Regression models appropriate for the PTE outcome were employed at both single and multiple levels to examine the associated factors and control for potential confounding variables.

A stepwise backward selection approach was employed to identify the optimal variables for inclusion in the regression models, utilizing a significance threshold of less than 0.2 (P value ≤ 0.2). Logistic regression was employed to assess the relationship between the occurrence of PTE and selected variables at both univariate and multivariate levels. The optimal multiple logistic regression model was determined using the area under the curve (AUC, ROC curve) and the Hosmer-Lemeshow test. The Hosmer-Lemeshow test was employed for model calibration.

Results

Demographics, clinical, and laboratory findings

This study involved 304 patients, who were selected based on the established entry and exclusion criteria, and subsequently divided into two equal groups of 152 individuals each. (Table 1 and 2) present the demographic, clinical, and laboratory findings of the patients. The mean age of the patients was 60.76 years, with a standard deviation of 16.59 years. No significant difference was observed in the age of patients between the two groups (P=0.105). Women comprised 51.97% of the patient population, and the gender distribution was consistent across both groups (P=0.357). Over 87% of patients were married, with no significant difference in marital status between the two groups (P=0.300). Analysis of the employment status of patients revealed that 55.92% were employed, 42.11% were housewives, and 1.97% were unemployed. No significant difference was observed in the occupational status of the patients between the two groups (P=0.473). No significant difference was observed in the drug history of patients between the two groups (P=1).

The body mass index in patients without pulmonary thromboembolism (28.36 kg/m²) was significantly higher than in those with pulmonary thromboembolism (28.06 kg/m²) (P<0.001). The assessment of hospital data across two groups indicated that patients in the PTE group experienced longer hospital stays (11.2 vs. 9.8 days, P=0.009) and higher rates of ICU admission (P<0.001) compared to the non-PTE group. Analysis of the clinical history of patients revealed that the prevalence of smoking in the PTE group was significantly greater than in the non-PTE group (P<0.001). Additionally, the frequency of individuals with chronic lung disease was notably higher in the PTE group (P=0.001).

Clinical symptoms and prognosis

Analysis of clinical symptoms in two groups revealed that individuals in the PTE group experienced a higher incidence of dyspnea (79.6% vs. 46.05%, P<0.001) and a lower prevalence of fatigue (28.95% vs. 40.13%, P=0.040) compared to the non-PTE group.

Analysis of hospitalization complications indicated that patients in the PTE group had a higher incidence of cardiac ischemia (25.66% vs. 15.79%, P=0.034) and deep vein thrombosis (DVT) (5.92% vs. 0%, P=0.003) when compared to the non-PTE group. The mortality rate in patients with PTE was significantly higher compared to those without PTE (P<0.001). Laboratory findings indicated that the number of lymphocytes in patients with PTE was significantly elevated compared to those without PTE (25.9 vs. 23.7, P=0.034). A significant relationship was observed between CRP levels and disease severity, with an increase in CRP 3+ noted in patients of the PTE group (P=0.04). In patients of the PTE group, troponin levels decreased significantly (P=0.023), while D-dimer (P<0.001) and ferritin levels (P<0.001) increased significantly.

Table 1- Demographic, clinical, and laboratory findings of hospitalized patients with or without PTE

Variables	P value	Non-PTE (n= 152)	PTE (n=152)	Total (n=304)
General information				
Age (years)	0.105	62.33 ± 17.00	63.94 ± 17.31	60.76 ± 16.59
Gender				
Female	0.357	138 (45.39)	65 (42.76)	73 (48.03)
Male		166 (54.61)	87 (57.24)	79 (51.97)
Marital status				
Married	0.300	254 (89.44)	127 (91.37)	127 (87.59)
Single		30 (10.56)	12 (8.63)	18 (12.41)
Job-status				
Employed	0.473	174 (57.24)	89 (58.55)	85 (55.92)
Housewife		121 (39.80)	57 (37.50)	64 (42.11)
Unemployed/retired		9 (2.96)	6 (3.95)	3 (1.97)
Body Mass Index (BMI, kg/cm^2)	<0.001*	28.06 ± 1.64	28.36 ± 1.87	27.76 ± 1.31
In-hospital information				
Length of hospital stay (days)	0.0009*	9.82 ± 6.54	11.17 ± 7.46	8.47 ± 5.14
ICU admission				
No	<0.001*	170 (55.92)	58 (38.16)	112 (73.86)
Yes		134 (44.08)	94 (61.84)	40 (26.32)
Habits and underlying diseases (Yes)				
Current smoker	<0.001*	40 (13.47)	33 (21.85)	7 (4.79)
Hypertension	0.896	79 (25.99)	39 (25.66)	40 (26.32)
Diabetes	0.882	55 (18.09)	27 (17.76)	28 (18.42)
Cardiovascular diseases	0.240	41 (13.49)	24 (15.79)	17 (11.18)
Dyslipidaemia	0.652	5 (1.64)	3 (1.97)	2 (1.32)

Chronic pulmonary diseases	0.001*	24 (7.89)	20 (13.16)	4 (2.63)
Chronic Kidney Diseases (CKD)	0.787	72 (23.86)	37 (24.34)	35 (23.03)
DVT/PTE	1.000	1 (0.33)	1 (0.66)	0 (0.00)
Stroke	1.000	2 (0.66)	1 (0.66)	1 (0.66)
Drug history (Yes)				
Anticoagulant	1.000	1 (0.33)	1 (0.66)	0 (0.00)
NOAC	N/A	0 (0.00)	0 (0.00)	0 (0.00)
Heparin	N/A	0 (0.00)	0 (0.00)	0 (0.00)

Data describes as n (%) or mean ± standard deviation, * statistically significant, P value < 0.05**,** N/A: Not Applicable.

Table 2- Clinical symptoms and prognosis of hospitalized COVID-19 patients with and without PTE

Variables	Non-PTE (n= 152)	PTE (n=152)	Total (n=304)	P value
The chief complaint in admission (Yes)				
Dyspnea	70 (46.05)	121 (79.61)	191 (62.83)	<0.001*
Chest pain	12 (7.89)	11 (7.24)	23 (7.57)	0.828
Cough	50 (32.89)	51 (33.55)	101 (33.22)	0.903
Fever	70 (46.05)	61 (40.13)	131 (43.09)	0.297
Leg pain	11 (7.24)	17 (11.18)	28 (9.21)	0.234
Fatigue	61 (40.13)	44 (28.95)	105 (34.54)	0.040*
Less of appetite	20 (13.16)	15 (9.87)	35 (11.51)	0.369
Loss of conscious	5 (3.29)	7 (4.61)	12 (3.95)	0.556
Interval of initial symptoms to admission (days)	5.08 ± 3.31	4.84 ± 3.15	4.96 ± 3.23	0.771
Complications during hospitalization (Yes)				
Cardiac ischemia	24 (15.79)	39 (25.66)	63 (20.72)	0.034*
Myocardial infarction	17 (11.18)	18 (11.84)	35 (11.51)	0.857
DVT	0 (0.00)	9 (5.92)	9 (2.96)	0.003*
Stroke	0 (0.00)	0 (0.00)	0 (0.00)	N/A
Vital status				
Expired	25 (16.45)	75 (49.34)	100 (32.89)	<0.001*
Alive	127 (83.55)	77 (50.66)	204 (67.11)	
Laboratory factors				
White Blood Cell count (WBC, 10^3/L)	8.32 ± 3.50	9.15 ± 4.63	8.73 ± 4.12	0.190
Lymphocyte (%)	23.73 ± 10.27	25.86 ± 11.45	24.80 ± 10.91	0.034*
Neutrophil (%)	72.15 ± 10.64	70.54 ± 10.96	71.34 ± 10.81	0.095
Neutrophil to Lymphocyte Ratio (NLR)	4.95 ± 8.18	4.81 ± 7.25	4.88 ± 7.71	0.051
C-reactive protein (CRP)				
1 +	48 (31.58)	33 (21.71)	81 (26.64)	0.040*
2 +	68 (44.74)	65 (42.76)	133 (43.75)	
3 +	36 (23.68)	54 (35.53)	90 (29.61)	
ESR (mm/hour)	33.96 ± 23.47	37.72 ± 27.87	35.82 ± 25.77	0.493
Troponin I (ng/ml)	0.16 ± 0.62	0.15 ± 0.79	0.15 ± 0.71	0.023*
D-dimer (ng/ml)	606.04 ± 656.86	4174.80 ± 1148.78	2396.31 ± 2017.09	<0.001*
Ferritin (ng/ml)	420.48 ± 322.65	1639.33 ± 514.38	1027.89 ± 745.71	<0.001*
Chest CT scan results:				
Involvement (%)	40.06 ± 20.82	58.17 ± 24.41	49.15 ± 24.41	<0.001*

Data describes as n (%) or mean ± standard deviation, * statistically significant, P value < 0.05**,** N/A: Not Applicable

Univariate and multivariate logistic regression models

(Table 3) presents the results of univariate and multivariate models predicting PTE based on D-dimer and ferritin factors. An independent examination of laboratory factors in relation to the occurrence of PTE revealed a significant relationship at the univariate level, with both factors (P<0.001). A 10-unit increase in the D-dimer factor corresponded to a significant 3% increase in the likelihood of PTE occurrence (95% CI=1.04-1.02, OR=1.03, P<0.001). Following an independent investigation into the predictive effect of ferritin on the incidence of PTE, it was noted that after adjusting for confounding variables, each 10-unit increase in ferritin was associated with a 6% increase in the likelihood of PTE occurrence (CI95%=1.04-1.07, OR=1.06, P<0.001) (Figure 1).

Table 3- The results of multivariate and logistic regression models in the relationship between D-dimer and ferritin with PTE

Factor	Model 1: Crude OR[1], 95% CI	P value	Model 2: Adjusted OR, 95% CI	P value	Model 3: Adjusted OR, 95% CI	P value
D-dimer (per 10 units)	1.02 (1.01 – 1.03)	<0.001*	1.03 (1.01 – 1.03)	<0.001*	1.03 (1.02 – 1.04)	<0.001*
Ferritin (per 10 units)	1.05 (1.04 – 1.07)	<0.001*	1.05 (1.04 – 1.07)	<0.001*	1.06 (1.04 – 1.07)	<0.001*

* statistically significant, P value < 0.05, [1]Odds ratio, 95% Confidence Interval, Model 1: intercept, D-dimer or ferritin, Model 2: intercept, gender, age, BMI, smoking, CT involvement, and D-dimer or ferritin, Model3: intercept, gender, age, BMI, smoking, CT involvement, NLR, CRP, history of chronic respiratory diseases, ICU admission, Length of hospital stay, occurrence of DVT during hospitalization, and D-dimer or ferritin

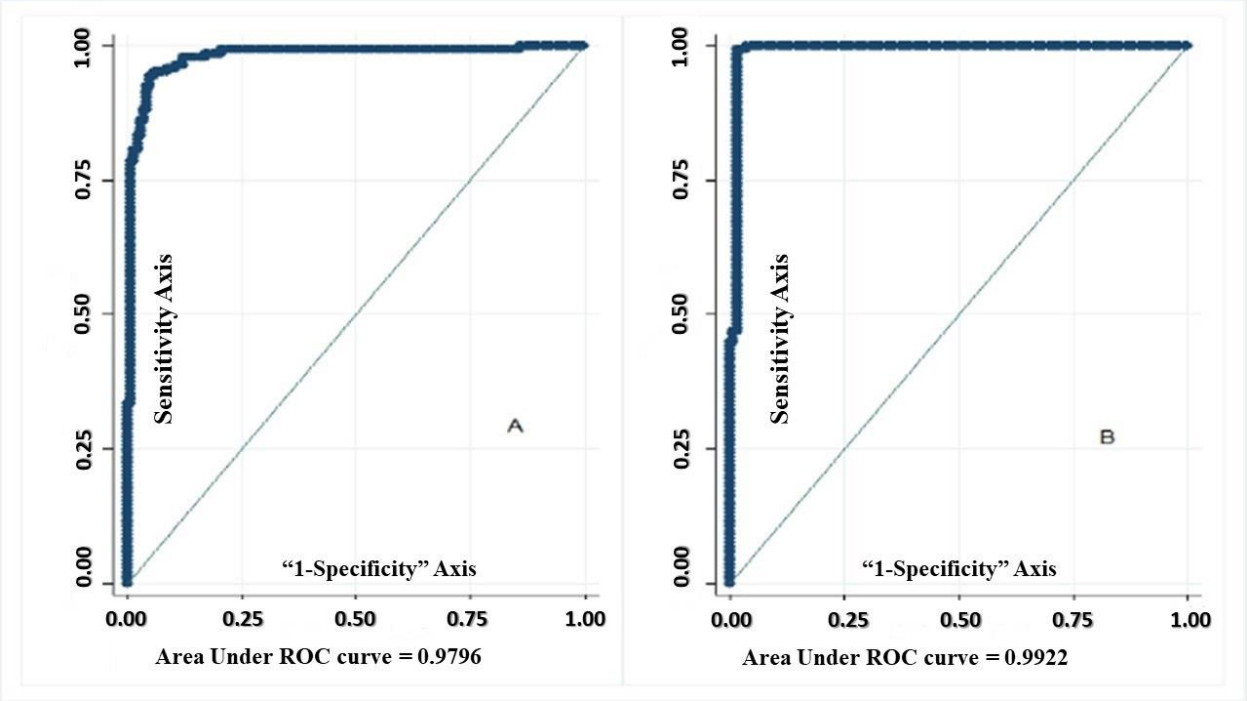

Figure 1- The rock curve indicator is one of the indicators of the model's ability to distinguish people who have experienced PTE from those who have not. According to the obtained results, the value of AUC for chart A, demonstrates the predicting effect of Ferritin in the likelihood of PTE occurrence

Discussion

The findings of our study indicated that, when comparing the PTE patient group to the non-PTE group, the variables of BMI (28.36 vs. 27.76), duration of hospitalization (11.2 days vs. 8.5 days), and ICU hospitalization rates (61.8% vs. 26.3%) were significantly elevated (P<0.05). PTE patients exhibited a higher prevalence of smoking (21.9% compared to 4.8%) and a history of chronic lung disease (13.2% versus 2.6%) with statistical significance (P<0.05). The evaluation of clinical characteristics in patients indicated an increased prevalence of dyspnea and fatigue among those with PTE. The most prevalent complications during hospitalization in patients included cardiac ischemia, myocardial infarction, DVT, and stroke. DVT prevalence was higher in the PTE group than in the non-PTE group. Laboratory results revealed a notable increase in lymphocytes and CRP levels in patients with PTE compared to those without PTE. A significant increase in ferritin level was observed in the PTE group compared to the Non-PTE group (OR=1.06, P<0.001). The ferritin level in patients with PTE was 3.9 times greater than that in non-PTE patients, measuring 1639.3 ng/ml compared to 420.5 ng/ml. Our results align with previous studies indicating that elevated ferritin and D-dimer levels correlate with disease severity and reduced survival in COVID-19 patients, thereby confirming our findings [4-6]. Ferritin serves as an acute phase reactant, exhibiting elevated levels in response to inflammatory and infectious diseases. Inflammation and infection are also features of COVID-19. There are multiple associations between ferritin and COVID-19. Initially, ferritin, functioning as an acute phase reactant, exhibits an increase in COVID-19 patients. Higher levels of ferritin

are associated with increased severity of COVID-19. Third, Ferritin has been linked to the duration of hospital stay and the period of viral clearance [8-9]. Fourth, elevated ferritin levels have been linked to an increased incidence of venous thromboembolism [10]. Additionally, ferritin has the potential to induce a cytokine storm [11]. Cytokine storm may lead to thromboembolic events, including pulmonary thromboembolism, in COVID-19 cases [12]. However, there is insufficient evidence to confirm its role in predicting mortality or thromboembolic events. Our findings indicate that elevated ferritin levels correlate with an increased incidence of PTE and mortality. This finding suggests that clinicians should regard elevated ferritin levels as warning signs that require more thorough evaluation and treatment [10].

An increase in D-dimer levels was observed in PTE patients (OR=1.03, P<0.001) compared to non-PTE patients. In our study, the average D-dimer level in the PTE group was 4174.80 ng/ml, while in the non-PTE group, it was 606.04 ng/ml, indicating an increase of 6.8 times. D-dimer is a sensitive biomarker for inflammation; however, it lacks specificity. The increase may occur due to various factors. Comorbidities, including diabetes and stroke, may also induce an increase in this biomarker. Consequently, the pathological role of D-dimer cannot be interpreted as straightforwardly as that of ferritin [13]. Our findings align with previous studies indicating that elevated D-dimer levels are associated with poor COVID-19 prognosis [14]. Previous research has indicated a correlation between D-dimer levels and pulmonary thromboembolism, supporting our findings [15]. Diabetes is a disease associated with inflammation and cardiovascular diseases [16-18]. Future research on the role of comorbidities of diabetes will be helpful.

Our findings may be incorporated into future research utilizing artificial intelligence to predict mortality associated with viral diseases. Incorporating additional variables, such as ferritin and D-dimer, which are linked to increased mortality in COVID-19 patients, has the potential to enhance the efficacy of artificial intelligence in clinical decision-making [19]. While prior research supports our findings [4-6], other studies indicate that D-dimer and ferritin levels do not correlate with PTE in COVID-19 patients [20]. Future original studies, systematic reviews, and meta-analyses on these markers may contribute to resolving this controversy.

Limitation

This study has limitations. While all laboratory findings recorded in the analysis pertain to the first 24 hours following patient arrival and prior to treatment initiation, co-morbidities or medications used for these conditions may influence the blood parameters. Furthermore, our study did not assess CT scan findings in the two groups of PTE and non-PTE patients.

Conclusion

This study demonstrated that elevated D-dimer levels, a nonspecific marker of coagulation issues, along with increased ferritin levels, may assist in identifying thromboembolism in patients with COVID-19. Predicting thromboembolism occurrence in the COVID-19 patient population facilitates improved identification of at-risk individuals and informs the prescription of anticoagulant therapy.

Ethics approval

This study was approved by the Research Council and the Ethics Committee of Shahid Beheshti University of Medical Sciences (ir.sbmu.msp.rec.1401.478).

References

[1] Lassau N, Ammari S, Chouzenoux E, Gortais H, Herent P, Devilder M, et al. Integrating deep learning CT-scan model, biological and clinical variables to predict severity of COVID-19 patients. Nat Commun. 2021;12(1):1-11.

[2] Zaim S, Chong JH, Sankaranarayanan V, Harky A. COVID-19 and multiorgan response. Curr Probl Cardiol. 2020;45(8):100618.

[3] Mueller AA, Tamura T, Crowley CP, DeGrado JR, Haider H, Jezmir JL, et al. Inflammatory biomarker trends predict respiratory decline in COVID-19 patients. Cell Rep Med. 2020;1(8).

[4] Huyut MT, Huyut Z. Effect of ferritin, INR, and D-dimer immunological parameters levels as predictors of COVID-19 mortality: A strong prediction with the decision trees. Heliyon. 2023;9(3).

[5] Sadeghi S, Nasirian M, Keivany E, Nasri P, Mirenayat MS. The demographic, clinical, and medical manifestations of pulmonary thromboembolism development in COVID-19. Blood Res. 2021;56(4):293-300.

[6] Sakr Y, Giovini M, Leone M, Pizzilli G, Kortgen A, Bauer M, et al. The clinical spectrum of pulmonary thromboembolism in patients with coronavirus disease-2019 (COVID-19) pneumonia: A European case series. J Crit Care. 2021;61:39-44.

[7] Lin S-h, Zhao Y-s, Zhou D-x, Zhou F-c, Xu F. Coronavirus disease 2019 (COVID-19): cytokine storms, hyper-inflammatory phenotypes, and acute respiratory distress syndrome. Genes Dis. 2020;7(4):520-7.

[8] Mahroum N, Alghory A, Kiyak Z, Alwani A, Seida R, Alrais M, Shoenfeld Y. Ferritin–from iron, through inflammation and autoimmunity, to COVID-19. J Autoimmun. 2022;126:102778.

[9] Cheng L, Li H, Li L, Liu C, Yan S, Chen H, Li Y. Ferritin in the coronavirus disease 2019 (COVID-

19): a systematic review and meta-analysis. J Clin Lab Anal. 2020;34(10):e23618.

[10] Liu H, Guo N, Zheng Q, Zhang Q, Chen J, Cai Y, et al. Association of interleukin-6, ferritin, and lactate dehydrogenase with venous thromboembolism in COVID-19: a systematic review and meta-analysis. BMC Infect Dis. 2024;24(1):324.

[11] Jia J, Wang M, Meng J, Ma Y, Wang Y, Miao N, et al. Ferritin triggers neutrophil extracellular trap-mediated cytokine storm through Msr1 contributing to adult-onset Still's disease pathogenesis. Nat Commun. 2022;13(1):6804.

[12] Middleton EA, He X-Y, Denorme F, Campbell RA, Ng D, Salvatore SP, et al. Neutrophil extracellular traps contribute to immunothrombosis in COVID-19 acute respiratory distress syndrome. Blood. 2020;136(10):1169-79.

[13] Ahmad F, Kannan M, Ansari AW. Role of SARS-CoV-2-induced cytokines and growth factors in coagulopathy and thromboembolism. Cytokine Growth Factor Rev. 2022; 63:58-68.

[14] Rostami M, Mansouritorghabeh H. D-dimer level in COVID-19 infection: a systematic review. Expert Rev Hematol. 2020;13(11):1265-75.

[15] Ventura-Díaz S, Quintana-Pérez JV, Gil-Boronat A, Herrero-Huertas M, Gorospe-Sarasúa L, Montilla J, et al. A higher D-dimer threshold for predicting pulmonary embolism in patients with COVID-19: a retrospective study. Emerg Radiol. 2020;27:679-89.

[16] Ebrahimi M, Ahmadieh H, Rezaei Kanavi M, Safi S, Alipour-Parsa S, Advani S, et al. Shared signaling pathways and comprehensive therapeutic approaches among diabetes complications. Front Med. 2025;11:1497750.

[17] Ebrahimi M, Fonarow GC. Higher Levels of Glucose within the Normal Range and Cardiovascular Risk: A Landscape Beyond Diabetes and Prediabetes. Am Heart J. 2025;. S0002-8703 (25) 00008-0.

[18] Omidi F, Sadeghi S, Kachoueian N, Ebrahimi M. A case report of diabetic ketoacidosis due to endocarditis of the mitral valve. Clin Case Rep. 2024;12(5):e8824.

[19] Reina-Reina A, Barrera JM, Maté A, Trujillo J, Valdivieso B, Gas M-E. Developing an interpretable machine learning model for predicting COVID-19 patients deteriorating prior to intensive care unit admission using laboratory markers. Heliyon. 2023;9(12).

[20] Mulder MM, Brandts L, Brüggemann RA, Koelmann M, Streng AS, Olie RH, et al. Serial markers of coagulation and inflammation and the occurrence of clinical pulmonary thromboembolism in mechanically ventilated patients with SARS-CoV-2 infection; the prospective Maastricht intensive care COVID cohort. Thromb J. 2021;19(1):35.