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The Relationship between the Results of Coagulation Profile and Severity of Pulmonary Involvement in COVID-19 Patients

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Abstract

Introduction: COVID-19 is currently a global pandemic, and coagulation-related mortality has been widely reported in patients suffering from it.

Objective: this article aimed to investigate the coagulation profile of COVID-19 patients.

Methods: This was a cross-sectional study conducted using a retrospective research design. We recruited patients with COVID-19 admitted to a hospital from June 15th to July 7th, 2020. Upon patients' entering a blood sample was drawn from each patient for assessing patient's coagulation profile (PT, PTT, INR, Platelet count); and a chest high-resolution computed tomography (HRCT) scan was performed for each patient. The study patients were divided in to sever group (CO-RADS score 5) and non-sever group (CO-RADS score <5).

Results: Thirty-six patients (20 males and 16 females) with a mean age of 54.7±17.5 years were studied. Of them, 11 cases (30.56%) had severe pulmonary involvement. Also, the coagulation profiles were longer in the severe group than non-sever group. As well, the means of platelet count that were 232.440 per microliter in the non-severe group and 289.180 per microliter in the severe and non-sever groups, respectively; but still not statistically significant ($p>0.05$). The Area under the ROC Curve (AUC) for PT and INR was 0.615 and 0.611, respectively. The AUC for platelet count was 0.680 (95% CI: 0.501 to 0.859) and had an acceptable discriminating power.

Conclusions: In this study, we did not find any statistically significant relationship between the results of coagulation tests and the severity of pulmonary involvement according to HRCT scan findings in COVID-19 patients. But further analyses suggest that, except PTT, the other coagulation tests (PT, INR, and platelet count) may discriminate severe COVID-19 patients.

Key words: Blood Coagulation; COVID-19; Lung; Severity of Illness Index

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INTRODUCTION

On 30 January 2020, the International Health Regulations (IHR) Emergency Committee of World Health Organization (WHO) declared a Public Health Emergency of International Concern (PHEIC) based on the growth rates in the reported COVID-19 cases in China and other regions of the world (1). The virus responsible for COVID-19 is a very pathogenic agent that primarily targets the human respiratory system (2). The clinical manifestations in these patients usually range from minor symptoms, such as fever and a dry cough that is sometimes accompanied by mild pneumonia and shortness of breath, to severe pneumonia, tachypnea, and disorders of gas exchange (3-5). About 5% of the patients with severe pulmonary involvement require mechanical ventilation and/or go into shock, and a large percentage of them suffer from multiple organ failure (6). There was some evidence indicating COVID-19 related abnormal level of coagulation markers and tests in the early reports from China. Han et al reported that preliminary characteristics of 99 patients admitted to hospitals in Wuhan showed that 6% had increased activated partial thromboplastin time (aPTT), 5% increased prothrombin time (PT), and 36% increased D-dimer and inflammatory

biomarkers including interleukin 6 (IL-6), increased erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) (7). Occurrence of some presentations such as frequent cardiovascular events in COVID-19 patients suggest that thrombotic events are probably involved in the disease course (8). But we are not aware that whether any relationship is present between the results of coagulation profile and severity of pulmonary involvement in COVID-19 patients or not? Therefore, this article aimed to investigate the coagulation profile of COVID-19 patients.

Methods

Study design and setting

This was a cross-sectional study conducted using a retrospective research design. COVID-19 patients admitted from June 15th to July 7th in Peymanieh Hospital, Jahrom, Iran were studied. Written informed consent was obtained from the participant. The study proposal was approved by the Ethics Committee of Jahrom University of Medical Sciences (IR.JUMS.REC.1398.130).

Study population

Data were collected by census method. Inclusion criteria encompassed patients with positive reverse transcription polymerase chain reaction (RT-PCR) test for COVID-19. Exclusion criteria were patient's lack of willingness to participate in the study or cooperate in the research until its end, and also history of underlying renal disease.

Data Collection

Upon patients' entering COVID-19 emergency department, 5 mL blood was drawn from each patient for routine electrolyte measurements and also assessing patient's coagulation profile (PT, PTT, INR, Platelet count); bedside blood glucose level was measured using a glucometer, and a chest high-resolution computed tomography (HRCT) scan was performed for each patient. An emergency medicine physician recorded the history of the underlying medical conditions and performed a physical examination.

Definition

The COVID-19 Reporting and Data System (CO-RADS) was used to evaluate the severity of pulmonary damage. It is a five-point-scale that has been proposed to demonstrate the degree of pulmonary involvement in COVID-19 patients. The level of suspicion for pulmonary involvement ranges from very low (CO-RADS 1) to very high (CO-RADS 5) (9). In this study, the study patients were divided in to sever group (CO-RADS score 5) and non-sever group (CO-RADS score <5).

Statistical Analysis

Continuous variables were presented as mean± standard deviation (SD) and median with interquartile range (IQR). We used the Chi-squared or Fisher's exact tests for assessing the distribution of categorical variables in the two groups based on CO-RADS categories <5 and 5. Also, the difference in the means of numerical variables in the two groups was assessed by Student's t-test. A p-value lower than 0.05 was considered statistically significant. The power of the coagulation tests to discriminate severe COVID-19 was assessed using the area under the ROC curve (AUC). The best cut-off point of platelet count for discriminating severe COVID-19 was determined using the J-Youden statistics. Sensitivity and specificity with a 95% confidence interval were presented for the best suggested cut-off point. All analyzes were performed using the STATA software version 15.

Results

Thirty-six patients (20 males and 16 females) with a mean age of 54.7±17.5 years were studied. Of them, 11 cases (30.56%) had severe pulmonary involvement based on HRCT scan findings (Figure 1). Table 1 presents demographic characteristics and presentation symptoms in the patients by CO-RADS category. Generally, the most common symptoms on admission were fever (55.6%), followed by shortness of breath (47.2%) and cough (41.7%).

Table 2 reports the means of assessed laboratory variables in the COVID-19 patients by CO-RADS category. The glucose (127.82 mg/dL vs 113.60 mg/dL) and BUN (19.45 mg/dL vs 17.60 mg/dL) levels were higher in severe patients than in the non-severe patients; However, the difference in CO-RADS categories was not statistically significant (p>0.05). Also, the coagulation profiles were longer in the severe group than non-sever group.

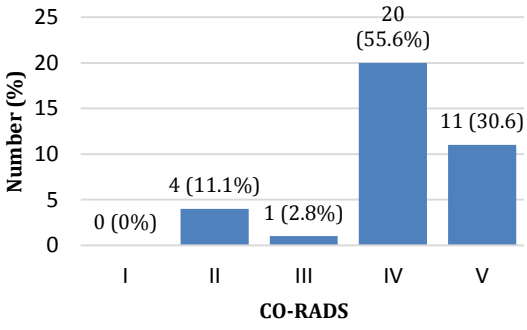

Figure 1: The distribution of studied COVID-19 patients according to CO-RADS categories.

Table 1: The basic characteristics and symptoms by CO-RADS category.

Variable	Total (n=36)	CO-RADS	
		<5 (n=25)	5 (n=11)
Age, Mean±SD	54.72±17.55	53.76±19.11	56.91±13.91
Age category, n (%)			
Under 30 years	2 (5.6)	2 (8.0)	0 (0.0)
30 to 60 years	20 (55.6)	14 (56.0)	6 (54.5)
Over 60 years	14 (38.9)	9 (36.0)	5 (45.5)
Sex, n (%)			
Male	20 (55.6)	14 (56.0)	6 (54.5)
Female	16 (44.4)	11 (44.0)	5 (45.5)
Symptoms, n (%)			
Cough	15 (41.7)	8 (32.0)	7 (63.6)
Shortness of breath	17 (47.2)	12 (48.0)	5 (45.5)
Fatigue	3 (8.3)	2 (8.0)	1 (9.1)
Fever	20 (55.6)	13 (52.0)	7 (63.6)
Abdominal pain	2 (5.6)	1 (4.0)	1 (9.1)
Gastroenteritis	2 (5.6)	2 (8.0)	0 (0.0)

Table 2: The differences in the means of laboratory variables in COVID-19 patients by CO-RADS category

Variable	Total (n=36)	CO-RADS		P-value
		<5 (n=25)	5 (n=11)	
Magnesium (Mg)	1.88±0.20	1.92±0.21	1.80±0.17)	0.115
Phosphor (P)	3.70±1.38	3.71±1.50	3.66±1.11	0.924
Blood urea nitrogen (BUN)	18.17±10.35	17.60±8.56	19.45±14.0	0.627
Creatinine (Cr)	1.39±0.88	1.38±0.92	1.44±0.80	0.852
Potassium (K)	4.10±0.57	4.08±0.61	4.14±0.28	0.802
Sodium (Na)	143.69±46.48	147.04±55.74	136.09±3.53	0.523
Albumin	3.36±0.39	3.34±0.43	3.38±0.30	0.793
Glucose	117.94±38.24	113.60±26.68	127.82±57.04	0.445
PT	14.72±1.44	14.57±1.41	15.05±1.52	0.361
PTT	31.97±6.39	31.72±7.07	32.52±4.74	0.737
INR	1.09±0.11	1.08±0.10	1.12±0.11	0.371
Platelets count	249.78±116.14	232.44±113.70	289.18±117.14	0.181

PT: prothrombin time; PTT: Partial thromboplastin time; INR: International normalized ratio

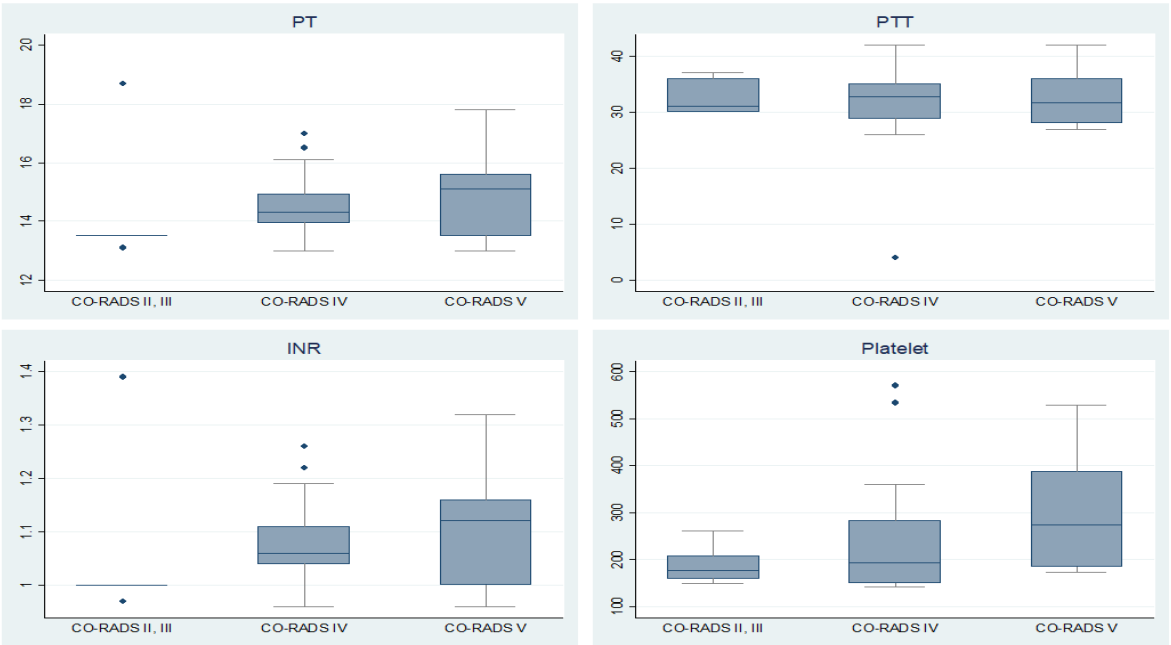

Figure 2: The distribution of coagulation marker levels by CO-RADS category

Table 3: The area under the ROC curve (with 95% CI) of coagulation markers for severe CO-RADS

Marker	AUC (95% CI)	P-value
PT	0.615 (0.404 to 825)	0.279
PTT	0.489 (0.277 to 0.701)	0.918
INR	0.611 (0.399 to 0.823)	0.295
Platelets count	0.680 (0.501 to 859)	0.089

PT: prothrombin time; PTT: Partial thromboplastin time; INR: International normalized ratio

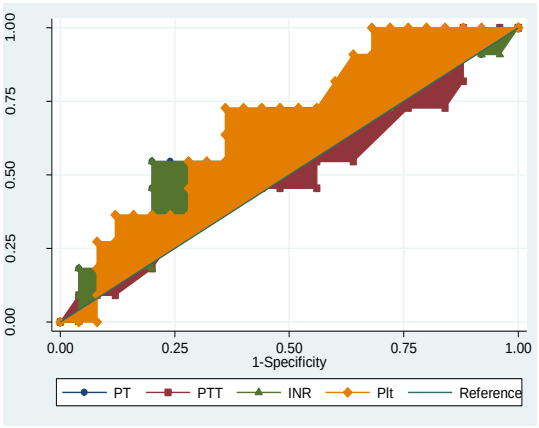

Figure 3: The area under the ROC curve of coagulation marker for severe CO-RADS

As well, the means of platelet count that were 232.440 per microliter in the non-severe group and 289.180 per microliter in the severe and non-sever groups, respectively; but still not statistically significant.

The Box plot of coagulation tests showed that the levels of all markers were higher in the severe patients (CO-RADS 5) compared to the mild ones (CO-RADS 2, 3) and moderate patients (CO-RADS 4) (Figure 2).

The median (interquartile range; IQR) of PT was 13.5 (2.8), 14.3 (1.1), and 15.1 (2.1) in mild, moderate, and severe groups, respectively. Also, the median (IQR) of the INR was 1.0 (0.21), 1.06 (0.07), and 1.12 (0.16) and for platelet count, it was 176.0 (81.0), 192.0 (138.3), 273.0 (201.0) in mild, moderate, and severe groups, respectively.

The area under the ROC curve of PTT was lower than that of the other tests and could not discriminate severe COVID-19 based on category 5 of CO-RADS. The AUC of PT and INR was 0.615 and 0.611, respectively. The AUC of platelet count was 0.680 (95% CI: 0.501 to 0.859) and had acceptable discrimination power (Table 3, Figure 3). The best cut-off point of platelet count for discriminating severe COVID-19 was >208,000 per microliter; and the sensitivity and specificity for this cut-off point were 72.73% (95% CI: 39.0% to 94.0%) and 64.0% (95% CI: 42.5% to 82.0%), respectively.

Discussion

In this study, we investigated the coagulation profile of COVID-19 patients and found that although there were some differences in severe and non-sever cases, but they were not statistically significant. However, except PTT, the other coagulation tests (PT, INR, and platelet count) may discriminate severe COVID-19 patients.

The study by Lodigiani et al. reported that coagulation and cardiac biomarkers increased in COVID-19 patients. This finding indicated inflammation manifested by coagulation activation and endothelial dysfunction (10). According to Zhou et al. findings, the complication rate in COVID-19 hospitalized patients for venous and arterial thromboembolism was approximately 8% despite anticoagulant prophylaxis (8). In contrast with Lodigiani's findings, significant relationship was not observed between the results of coagulation tests and the severity of pulmonary involvement in COVID-19 patients in the present study. However, there may be dissimilarities between the results due to geographical and ethnic differences between our patients and those examined by Lodigiani. In another study, it was reported that the difference in the median levels of D-dimer was higher between non-surviving and surviving COVID-19 patients than between acute respiratory distress syndrome (ARDS) and non-ARDS patients; It indicates that disseminated intravascular coagulation (DIC)-related complications may lead to death in a subset of COVID-19 patients independently of ARDS (11). In the present study, D-dimer levels were not available for all patients because, during the first peak of COVID-19 in Iran, in which the number of patients was low, this marker was not routinely tested. On the other hand, the study by Liu et al. showed no significant correlation between COVID-19 and thrombocytopenia (12). In the present study, the mean platelet count was a bit higher in patients with higher CO-RADS scores, which somehow in line with the results of the study by Liu et al. One recent report has suggested that immune thrombocytopenia (ITP) may be associated with COVID-19 infection (13). ITP is a rare autoimmune disease, characterized by a platelet count of < 100 × 109/L, that increases the risk of internal bleeding (14). ITP has been reported not only during active COVID-19 infection but also up to 10 days after the clinical COVID-19 symptoms have subsided. Diagnosis of COVID-19-related ITP may be difficult due to several other potential factors, including coagulation activation by COVID-19 which leads to DIC and subsequent thrombocytopenia. Also,

suggested treatments for COVID-19 such as heparin, azithromycin, and hydroxychloroquine may cause thrombocytopenia (15, 16).

Limitations

The small sample size of the present study is its main limitation. As a result, we found wide confidence intervals for AUC and other indices such as sensitivity and specificity. Therefore, the result of this study should be interpreted with caution and a larger sample size study is needed to confirm or disprove the hypothesis presented in this study.

Conclusions

In this study, we did not find any statistically significant relationship between the results of coagulation tests and the severity of pulmonary involvement according to HRCT scan findings in COVID-19 patients. But further analyses suggest that, except PTT, the other coagulation tests may discriminate severe COVID-19 patients.

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Authors' contribution

All the authors met the standards of authorship based on the recommendations of the International Committee of Medical Journal Editors.

Conflict of interest

None declared.

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