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Parameters of Coagulation in COVID-19 Patients: A Correlation with Clinical Severity

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ABSTRACT

Introduction: COVID-19 infection can be complicated by coagulation derangement and a high risk of thromboembolic episodes. Our study aimed to investigate coagulation parameters in COVID-19 patients and their correlation with clinical severity. **Methods:** We analyzed coagulation parameters PT, APTT, D-Dimer, and Fibrinogen in 98 RT-PCR-confirmed COVID-19 patients admitted to the Government Institute of Medical Sciences, Gautam Buddha Nagar, Uttar Pradesh, India. **Results:** This study involved 69 males (70.50%), and 29 (29.5%) were females. The mortality rate was 6.12% (n= 06). Forty-six patients (46.94%) had comorbidities. Thirty-four patients had elevated PT, and 7 had high APTT, whereas D-dimer and fibrinogen levels were raised in 68 and 61 patients, respectively. Among all four parameters, D-Dimer levels were significantly associated with disease severity. **Conclusion:** Derangement of D-dimer levels is significantly associated with disease severity in COVID-19 infection.

INTRODUCTION

In late 2019, a novel coronavirus disease (COVID-19) emerged in Wuhan, China casting its ominous appearance on the eastern part of the globe. Due to its rapid spread in a few months, it infected millions worldwide, with many losing their lives since the pandemic occurred [1].

Research showed that the novel coronavirus disease was similar to severe acute and middle-east respiratory syndromes [2]. It is typically known to spread via the respiratory route through droplets and close contact causing fever, dry cough, sore throat, running nose, and loss of smell and taste [3, 4]. Most patients are known to have good prognoses, but in a few, it progresses rapidly into severe respiratory distress, coagulation dysfunction, and multiple organ failure [5]. COVID-19 can lead to coagulation disorder resulting from endothelial damage, inappropriate coagulation pathway activation, and intravascular fibrin deposition. Serious sequelae like thrombus formation and DIC have also been reported in severely affected patients [6].

Among the various clinical and biochemical parameters associated with poor prognosis, increased D- dimer and fibrinogen levels have gained particular attention as a predictor of the development of acute respiratory distress syndrome, admission to the intensive care unit, or death [7]. Hence commonly used clinical lab coagulation markers such as D-dimer, prothrombin time (PT), activated partial thromboplastin time (APTT), thrombin time (TT), and fibrinogen could subtly predict the predisposition to thrombosis.

A study to evaluate parameters of coagulation and their correlation with clinical severity in COVID-19 patients was undertaken at our hospital, a tertiary care institution in Western Uttar Pradesh.

MATERIAL AND METHODS

The present ambispective included COVID-1998 patients with a positive RT-PCR test admitted to the Government Institute of Medical Sciences, Greater Noida, from June 2020 to September 2020. Case files in Medical Record Division were gathered, and relevant details were recorded, including medical history, physical examination findings, and laboratory investigations. The Institutional

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Ethics Committee reviewed and approved this study as per the letter no GIMS/IEC/HR/2020/25. The patients were classified as mild, moderate, and severe as per MoHFW guidelines on presentation [8]. Laboratory parameters, including prothrombin time (PT), activated partial thromboplastin time (APTT), D-dimer and fibrinogen, were run on an automated coagulometer stage machine. The normal range for PT, APTT, fibrinogen, and D dimer was 11 to 16 seconds, 25 to 40 seconds, 180 to 360 mg/dl, and 0 to 0.5mg/dl, respectively [9]. Clinical outcome indicators were excluded from the hospital and deaths.

Statistical analysis was performed using SPSS 15.0 (SPSS Inc, Chicago, USA). The Chi-square test and percentage proportions were performed to find the correlation between coagulation parameters in COVID-19 patients and disease severity. P <0.05 was considered statistically significant.

RESULTS

Ninety-eight patients were included in the present study, of which 29 (29.5%) were female, and 69 (70.5%) were males. At admission, 42 patients (42.85%) presented mild symptoms, and 28 (28.57%), were assigned to moderate and severe groups. The mortality rate in the present study was 6.12 % (n=06). The mean ages for the mild, moderate, and severe subsets were 38.74±16.5 years (25 males and 17 females), 55.64±13.3 years (20 males and 8 females), and 50.83±15.3 years (24 males and 4 females), respectively (Table 1). Patients were categorized into three age groups, i.e., 18-36 years, 37-72 years, and above 72 years.

Forty-two (42.85%) patients were in the mild clinical category, followed by 28 in moderate and 28 in severe groups (Table 1). Out of the total 28 patients in the severe category, 67.85% (n=19) were 37-72 years old. Mortality was 66.67% (4 of total 6 deaths) among the age group of 37-72 years. All deaths occurred in the severe category.

Among the patients requiring ICU care (n=36), 25 (69.4%) were in the age group 37-72 years. Nine ICU patients (25%) required intubation, and six (66.67%) were 37-72 years old.

Fifty-two patients (53.06%) had no comorbidity history, while 46 (46.94%) had comorbidities, namely diabetes mellitus, hypertension, and tuberculosis. The most common comorbidity was hypertension (n=26, 56.52%), followed by 25 cases of diabetes mellitus (54.34%), ten hypothyroidism (21.73%), four each of coronary artery disease and chronic kidney disease (8.69%) and one case of tuberculosis (2.17%). Twenty-three patients had both diabetes and hypertension. Comorbidities coexisted in 57.14% (n =24) of mild and 57% (n=16) of the moderate and severe category patients. Comorbidities coexisted in fifty percent of cases with mortality (n= 03).

Out of 98 cases studied, we found 34 patients (35%) had elevated PT, and 7 (7%) had high APTT values. Of the 28 patients with severe disease, 7 (25%) had high PT, and 2(7%) presented with elevated APTT levels. The value of PT and APTT was not significantly related to the severity of the disease of COVID-19 patients (P>0.05). (Table 2)

D-dimer and fibrinogen levels were raised in 68 and 61 patients, respectively. Among 68 patients with raised D-dimer, 25 (36.76%) belonged to the severe clinical category, while raised fibrinogen levels were demonstrated in 20 (32.78%) of the 61 patients in the severe category. D-dimer and fibrinogen levels were elevated in 6 (100%) and 4 (66.67%) non-survival patients. The D-dimer value was correlated significantly with the severity of the disease (P=0.018). On the other hand, fibrinogen level was not significantly related to the severity of the disease in COVID-19 patients (Table 2).

Table 1. COVID-19 vs. severity

Age group (years)	Mild	Moderate	Severe	Death
18-36	23	2	05	01
37-72	18	23	19	04
>72	01	03	04	01
Total	42	28	28	06

Coagulation parameters studied included PT, APTT, D-dimer, and fibrinogen.

Table 2. Coagulation parameters vs. COVID-19 severity.

S.No.	Parameter	Range	Result	Mild	Moderate	Severe	Total	*P*-value
1	PT	11-16 Seconds	Normal	27	16	21	64	0.36
			Deranged	15	12	7	34	
2	APTT	25-40 Seconds	Normal	39	26	26	91	1
			Deranged	3	2	2	7	
3	D-Dimer	0-0.50 mg/dl	Normal	19	8	3	30	0.018
			Deranged	23	20	25	68	
4	Fibrinogen	180-360 mg/dl	Normal	22	7	8	37	0.127
			Deranged	20	21	20	61	

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DISCUSSION

The coagulation profile is dysfunctional in COVID-19 patients. Two surveys have reported altered coagulation profiles in COVID-19 patients [10, 11]. In the present study, male patients (n=69, 70.50%) outnumbered female patients, concordant with other reports [12, 13]. Patients in the 37-72 years age group were affected mainly in terms of severity, admission to ICU, the requirement for intubation, and mortality.

The most common comorbidity in the present study was hypertension (n=26), followed by diabetes mellitus (n=25), a finding also reported in a similar study [14].

Few authors have also reported increased prothrombin time in COVID-19 patients, which is inconsistent with our findings [2,12]. On the other hand, some authors reported prolonged prothrombin time and low fibrinogen levels in COVID-19 patients [10,11], which correlate with disease severity. In the present study, we found prothrombin time elevated in the maximum number of patients (n=15) with mild COVID-19 symptoms and 12 and 7 cases, respectively, of the moderate and severe categories (P = 0.36). Chen *et al.* (2019) and Han *et al.* (2020) found no significant correlation between COVID-19 disease severity and coagulation profile [15, 16].

APTT was in the normal range in all the clinical severity groups (P=01) in our study. The same was also reported by [2]. PT and APTT not being significantly elevated in the present study explain the absence of bleeding tendency in the patients.

We found D-dimer significantly associated with disease severity in the present study (P=0.018). D-dimer was significantly deranged in the four morbid patients in the severe clinical category. Likewise, some studies [12-14] have documented statistically raised levels of D-dimer associated with severe and critically ill patients.

Xin Jin *et al*. [2] reported increased fibrinogen levels in COVID-19 patients responsible for the increased tendency for thrombosis. This was not found significant in our study (P = 0.127). Few studies suggest that COVID-19 infection causes endothelial cell injury, leading to fibrinolytic system activation, which explains the increased D-dimer in severe COVID-19 patients [17,18].

The present study reconfirms that COVID-19 infection leads to coagulopathy as indicated by elevated D-dimer levels in severely affected patients entailing a poor prognosis. Evaluation of coagulation parameters in the patients early on admission can guide treating physicians regarding prognosis and choices in therapy.

One of the limitations of this study was that it was a single-center study having relatively few subjects. More extensive studies may throw more light on the conclusions drawn.

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CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest associated with this manuscript.

REFERENCES

1. World health organization, Novel Coronavirus (Covid-19) situation. Available: https://covid19.who.int/
2. Jin X, Duan Y, Bao T, Gu J, Chen Y, Li Y, et al. The values of coagulation function in COVID-19 patients. PLoS One. 2020; 15 (10): e0241329.
3. W.J.Guan, Z.Y.Ni, Y.Hu, W.H Liang, C.Q Ou, J.x He, et al. Clinical characteristics of coronavirus disease 2019 in China. NEJM. 2020; 382 (18): 1708-20.
4. Hui DS, I Azhar E, Madani TA, Ntoumi F, Kock R, Dar O, et al. The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health - The latest 2019 novel coronavirus outbreak in Wuhan China. Int J Infect Dis. 2020; 91: 264-6
5. Wu F, Zhao S, Yu B, Chen YM, Wang W, Song ZG et al. A new coronavirus associated with human respiratory disease in China. Nature. 2020; 3 (10): 265-9.
6. Han W, Quan B, Guo Y, Zhang J, Lu Y, Feng G, et al. The course of clinical diagnosis and treatment of a case infected with coronavirus disease 2019. J Med Virol. 2020; 92 (5): 461-3.
7. Tang N, Li D, Wang X, Sun Z. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. J Thromb Haemost. 2020; 18 (4): 844-7.
8. Clinical Management Protocol: Covid-19. Version-3: Mohfw. 13.06.2020.
9. Dacie and Lewis Practical Hematology. 12th Edition: Barbara J Bain, Imelda Bates, Michael A. Laffan; 2017.
10. Tang N, Li D, Wang X, Sun Z. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. J Thromb Haemost. 2020; 18 (4): 844-7.
11. Giannis D, Ziogas IA, Gianni P. Coagulation disorders in coronavirus infected patients: COVID-19, SARS-CoV-1, MERS-CoV and lessons from the past. J Clin Virol. 2020; 127: 104362.
12. Long H, Nie L, Xiang X, Li H, Zhang X, Fu X, et al. D-Dimer and Prothrombin Time Are the Significant Indicators of Severe COVID-19 and Poor Prognosis. Biomed Res Int. 2020; 2020: 6159720.
13. Martín-Rojas RM, Pérez-Rus G, Delgado-Pinos VE, Domingo-González A, Regalado-Artamendi I, Alba-Urdiales N, et al. COVID-19 coagulopathy: An in-depth analysis of the coagulation system. Eur J Haematol. 2020; 105 (6): 741-50.
14. Luo HC, You CY, Lu SW, Fu YQ. Characteristics of coagulation alteration in patients with COVID-19. Ann Hematol. 2021; 100 (1): 45-52.
15. Chen G, Wu D, Guo W, Cao Y, Huang D, Wang H, et al. Clinical and immunologic features in severe and moderate coronavirus disease 2019. J Clin Invest. 2020; 130 (5): 2620-9.

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16. Han H, Yang L, Liu R, Liu F, Wu KL, Li J, et al. Prominent changes in blood coagulation of patients with SARS-CoV-2 infection. Clin Chem Lab Med. 2020; 58: 1116-20.

17. Whyte CS, Morrow GB, Mitchell JL, Chowdary P, Mutch NJ. Fibrinolytic abnormalities in acute respiratory distress syndrome (ARDS) and versatility of thrombolytic drugs to treat COVID-19. J Thromb Haemost. 2020; 18 (7): 1548-55.

18. Ozolina A, Sarkele M, Sabelnikovs O, Skesters A, Jaunalksne I, Serova J, et al. Activation of Coagulation and Fibrinolysis in Acute Respiratory Distress Syndrome: A Prospective Pilot Study. Front Med (Lausanne). 2016; 28; 3: 64.

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