

A STUDY ON COAGULATION PROFILE OF COVID POSITIVE PATIENTS WITH CT CHANGES

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ABSTRACT

More than 25.3 million people have been impacted by the current pandemic since COVID-19 (coronavirus disease) had been first noticed in Wuhan, China in 2019. Individuals who are at elevated risk as well as show more than one manifestation in addition to pulmonary complications have a high death rate [1-3]. In individuals with COVID-19, coagulation abnormalities are commonly observed and are linked to a poorer prognosis and survival rate. Elevated D-dimer levels had been consistently correlated with worse results as well as mortality. Prothrombin time (P.T.) extension has also been observed under extreme circumstances, along with it occurring in non-survivors more commonly. Phenol levels can rise to their maximum limits during the acute reaction to the infection and remain there as the disease progresses; however, in a group of patients suffering from coronavirus pneumonia, before death, there has been a noted reduction in these levels [4]. Hematological abnormalities in patients suffering from COVID-19 point to a procoagulant state associated with venous and arterial thrombosis, which was more commonly noted in situations of severe cases [5-6]. VTEs (Venous thromboembolic events) happened in 2.9percent of 138 COVID-19 patients, according to a Chinese study. Nonetheless, in a small group of really ill patients admitted to the ICU, the VTE rate had been 20percent. When the pulmonary embolism rates in a single centre in France had been contrasted among general patients of ICU from the prior year and ICU admissions due to COVID-19 in 2020, the results showed rates of 20.6% and 6.1%, respectively. Up to 50percent of patients with severe COVID-19 symptoms have been documented to have coagulopathy, and over 70percent of cases have been found to have disseminated intravascular coagulopathy. Because prophylactic therapy appears to lower mortality from coagulation abnormalities, it has been recommended for hospitalized patients.

INTRODUCTION

However, in several instances, COVID-19 patients have been diagnosed with pulmonary embolism even after receiving the standard pharmacological thromboprophylaxis. Therefore, in some cases, anticoagulation may not be sufficient, and additional or alternative therapy may be needed. It may be useful to monitor hemostatic markers in all COVID-19 patients, as aberrant coagulation parameters may be linked to a poor prognosis. This illness mostly impacts the respiratory system as well as is transmitted through aerosols emitted while coughing as well as sneezing. The primary manifestations of COVID-19 have been rhinorrhea, myalgia, cephalalgia, productive cough, dyspnea, nasal obstruction, as well as pyrexia [7-8]. PCR (polymerase chain reaction) positive, Clinical symptoms, as well as the presence of ground-glass opacities on CT (computed tomography) scans, are primary diagnostic criteria for this disease. Recent research has examined the significance of serum inflammatory markers, including lymphocyte counts, homocysteine, CRP (C- reactive protein), along D-dimer levels, in predicting the development of COVID-19.

Severe patients of COVID-19 have higher ferritin levels, an important immune response mediator. A cytokine storm could result from elevated ferritin's direct proinflammatory and immunosuppressive effects. Vitamin D stimulates the production of anti-microbial peptides through its effect on the nuclear vitamin D receptor, hence enhancing innate cellular immunity. Patients with viral pneumonia have been observed to have lower levels of vitamin D. Vitamin D is known to decline the risk of viral infections through a number of procedures.

The fibrin degradation product D-dimer is utilized to eliminate the thrombosis diagnosis. Severe COVID-19 cases have been linked to elevated D-dimer value, microangiopathy, and hypercoagulability. Recent otolaryngology research has concentrated on the

correlation among anosmia as well as dysgeusia symptoms in the formation of minimal-to-mild COVID-19, along with the standard COVID-19 symptoms [9]. It is simple to do and doesn't require any intervention to assess those symptoms. According to Yan et al., people with taste abnormalities are ten times more likely to contract COVID-19. Nevertheless, there is insufficient data to determine if serum marker levels that indicate the severity of the disease and dysgeusia

symptoms are related. [10]. The aim of this investigation is to find out how useful coagulation indicators, including serum fibrinogen, activated partial thromboplastin time, prothrombin time, & D-dimer, are in predicting the degree of CT changes associated with the infection of COVID-19.

MATERIALS AND METHODS

This investigation had been conducted at the Saveetha Medical College Hospital from February 2021 to December 2021. Participants who met the study's participation requirements were chosen after receiving prior institutional ethical clearance and giving their informed consent. Men and women between the ages of 18 and 70 who had positive COVID-19 RTPCR tests and agreed to take part in the study were enrolled. Patients with a history of interstitial lung diseases, lung malignancy, tuberculosis, atelectasis, any bleeding diathesis, treatment for the same, or any anticoagulant therapy or lobectomy were excluded from the study. A predesigned and pretested proforma containing multiple socioeconomic variables such as age, sex, occupation, religion, and so forth was used to collect the data for the study. The simple random sample method was employed to select about 50 cases. Included were fifty patients who were admitted to Saveetha Medical College Hospital as well as had confirmed COVID-19. In connection with C.T. imaging, clinical classifications, and severity, the dynamic variations of D-dimer, prothrombin time, activated partial thromboplastin time, as well as serum fibrinogen had been analyzed along examined. The SARS-CoV-2 nucleic acid test, performed by real-time fluorescence RT-PCR, yielded a positive result for the concerned patients. Picture Archiving and Communication Systems were utilized to gather and assess the high-resolution CT images of the chest (PACS). On the day of the patient's presentation, all initial chest HRCT scans will be carried out, and images will be analyzed to determine each patient's disease severity score. First, the scans were evaluated for typical COVID-19 pneumonia abnormalities (bilateral, multilobe, posterior peripheral ground-glass opacities), as described by the RSNA Consensus Statement, regardless of whether they were positive or negative. The following scoring system will then be used to determine the severity, and it will be based on the visual evaluation of each implicated lobe: Lobar involvement percentage: 5% or less a score of 1;

5%-25% a score of 2, for 26%-49% a score of 3, for 50 percent-75 percent score of 4 and for more than 75 percent a score of 5. Its overall severity is indicated by the total of these lobar scores: a total score of seven or less was graded mild, a score between 8 and 17 was graded moderate, and a score of 18 or more was graded severe. SPSS 21.0 was employed to conduct the statistical analysis.

Numbers and relative frequencies were used to describe the clinical, demographic, and laboratory results for the patients in descriptive statistics. C.T. score frequencies were computed and compared to other clinical factors. For correlations, Pearson correlation coefficient tests had been utilized, as well as statistical significance had been determined by a p-value of <0.05.

RESULTS

Approximately 42% of the individuals in this study were between the ages of 41 and 60. Thirty percent of the population was over sixty years old, while sixteen percent was between the ages of twenty to forty. Approximately 12% of the individuals belonged to the age category of under 20 years. The average age is 55.24 as well as SD is 3.82 as mentioned in table 1 (Table 1). About 68% were males and 32% were females in our study. From table 2 we can infer that about 56% were smokers, 56% were diabetics, 48% were hypertensives, 52% had bronchial asthma and 24% had cardiovascular disease (Table 2). Table 3 shows that the patients presented with a variety of symptoms the most common one being fever seen in 88% of participants followed by cough seen in 84% of the patients (Table 3). The current study found that approximately 36% of individuals experienced a mild COVID-19 infection, 44% experienced a moderate COVID-19 infection, and 20% experienced a severe COVID-19 infection. The mean d-dimer value of severe COVID-19 infection is greater than the d-dimer value of mild and moderate infection of COVID-19. Table 4 states that there is a statistically significant correlation ($P < 0.05$) among d-dimer levels along the extent of COVID-19 infection. According to Table 5, the mean prothrombin time of a severe COVID-19 infection is greater than the mean prothrombin time of a mild or moderate infection of COVID-19. Prothrombin time is statistically significantly correlated with the COVID-19 infection's severity. Table 6 shows that there is no statistically significant association among the severity of COVID-19 infection and activated partial thromboplastin time. Similarly, as per the data in Table 7, we can observe that there is no significant association between fibrinogen and severity of infection (Tables 4,5,6,7).

DISCUSSION

COVID-19 has been spreading worldwide since December 2019. The disease's initial stages are linked with high D-dimer levels as well as prolonged PT, indicating coagulation pathway activation and thrombosis. The degree of D-dimer rise in COVID-19 patients is associated with a greater rate of mortality. The lungs of COVID-19 patients showed severe interstitial and alveolar inflammation. Numerous symptoms are caused by COVID-19, and the hemostatic system is often involved. Early in the course of the illness, pulmonary thrombosis may result from severe pulmonary inflammation, which promotes pulmonary vascular activation as well as destruction [11]. It is more likely that the strong inflammatory response is caused by COVID-19 and endothelial activation or damage than the intrinsic procoagulant properties of the SARS-CoV-2 virus which cause coagulopathy. Recent COVID-19 autopsy findings show enhanced angiogenesis, increased capillary microthrombi, pulmonary endothelial viral inclusions, and death [12]. Three phases have been identified in COVID-19-associated coagulopathy: Stage-1 is

characterized by raised D-dimer; Stage-2 is characterized by elevated D-dimer together with mildly extended PT/ INR, aPTT, as well as mild thrombocytopenia; & Stage-3 is characterized by acute illness as well as the laboratory examine that advance towards classic DIC. Elevated D-dimers had been depicted to be an independent biomarker for a poor prognosis, even in COVID-19 patients receiving

LMWH. D-dimers are greatly raised in COVID-19, possibly indicating pulmonary vascular bed thrombosis as well as fibrinolysis. D-dimer represents fibrin clot formation, fibrinolysis, and clot crosslinking by FXIIIa [13-15]. The elevated D-dimer level observed in COVID-19 could be attributed to coagulation activation brought on by viremia and cytokine storms, while superinfection along with organ failure are also potential causes. D-dimer cut-off values greater than 0.5g/mL in COVID-19 patients may indicate a higher probability of unfavorable outcomes [16]. Elevations in D-dimer values indicate a worsening of the COVID-19 infection and will likely require more severe critical care. In the present study, about 36% had a mild COVID-19 infection, 44% had a

moderate rate of COVID-19 infection, along with 20% had a severe rate of COVID-19 infection. When comparing it to mild and moderate COVID-19 infections, the mean d-dimer value of a severe COVID-19 infection is greater.

A statistically significant correlation ($P<0.05$) has been seen between the level of CT changes in COVID-19 infection as well as D-dimer. The mean prothrombin time of severe COVID-19 infection is greater than the mean prothrombin time of mild and moderate COVID-19 infection. Prothrombin time and the severity of CT alterations in COVID-19 infection as well as statistically significantly correlated ($P<0.05$). $P>0.05$ depicts that there is no statistically significant correlation among the severity of CT changes in COVID-19 infection and activated partial thromboplastin time. There is statistically no significant association among fibrinogen as well as the severity of CT changes in COVID-19 infection. In 1,500 COVID-19 hospital admissions, Li et al. found that age (OR 1.18; 95 percent CI 1.02-1.36) as well as baseline D-dimer level (OR 3.18; 95 percent CI 1.48-6.82) increased death risk. [17]. An elevated D-dimer $>1.0\text{g/mL}$ (FEU or DDU units not mentioned) upon admission and increased PT were related to death, according to Zhou et al. Tang et al. observed that 71.4percent of non-survivors and 0.6percent of recovered patients had disseminated intravascular coagulation throughout hospitalization in 183 patients [18-19]. 14 Autopsy findings from Italy showed fibrin thrombi in pulmonary minor artery arteries in

87percent of the fatal cases studied, suggesting a role for coagulation in diffuse endothelial as well as alveolar damage [20]. These results effectively demonstrate the hypercoagulability of severe COVID-19 patients. Elevated D-dimer levels upon admission and a sharp rise in D-dimer levels (3-to 4-fold) over time as well as “associated with high mortality. These findings may suggest coagulation activation because of infection or sepsis, a cytokine storm, or imminent organ failure. In addition, COVID-19 induces microvascular thrombotic diseases (as often reported at autopsy in the pulmonary vascular beds) and thrombotic events in the arteries (strokes, ischemia limbs). Serious bleeding events are rare in COVID-19 patients, as is disseminated intravascular coagulopathy (DIC). The COVID-19 severity and prognosis are challenging to determine due to the wide range of symptoms, radiological findings, and disease progression. ACE-2 is a membrane protein that is present in blood vessels, the heart, the kidneys, the” lungs, as well as many other organs. It is the principal receptor used by the SARS-Cov2 virus. The binding of SARS-CoV-2 to ACE-2 results in endothelial damage, a pro- and anticoagulant signal imbalance, and a localized and systemic inflammatory response, which in turn induces macro- and microvascular thrombosis. As a result, detecting and correcting coagulation malfunctions early on could significantly reduce mortality. D-dimer, PT, and APTT are examples of common laboratory coagulation markers. The increased fibrinolytic activity of the bodily system indicates a hypercoagulating condition and secondary fibrinolysis in the presence of elevated D-dimer levels. Exogenous as well as endogenous coagulation system factors, PT and APTT, respectively, can cause bleeding.

CONCLUSION

Based on our study, coagulation abnormalities in terms of D-dimer as well as prothrombin time have a considerable association with the severity of CT changes in COVID-19 pneumonia. Thus, it is important to monitor D-dimer and prothrombin time at the time of presentation. Preventive steps may be helpful in lowering the risk of DIC and thromboembolism due to coagulation disorders which will lower the morbidity as well as mortality rate of COVID-19-infected patients.

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TABLES

Age in years	Frequency	Percentage	Mean $\pm$ S.D
0-20 years	6	12	
21-40 years	8	16	
41-60 years	21	42	55.24 $\pm$ 3.82
>60 years	15	30	
Total	50	100	

Table 1: Agewise distribution of study participants

Risk factors	Frequency	Percentage
Smoking	28	56
Diabetes Mellitus	28	56
Hypertension	24	48
Bronchial asthma	26	52
Cardiovascular disease	12	24

Table 2: Risk factors among study participants

Clinical features	Frequency	Percentage
Fever	44	88
Cough	42	84
Arthralgia	20	40
Headache	24	48
GIT symptoms	18	36

Table 3: Symptom wise distribution among study participants

Severity	Mean (mg/l)	SD	P value
Mild	0.85	1.68	0.01
Moderate	1.78	4.40	
Severe	3.86	5.23	

Table 4: Association between d-dimer and severity of covid 19 infection

Severity	Mean (sec)	SD	P value
Mild	10.34	1.91	0.01
Moderate	12.14	1.16	
Severe	13.70	3.38	

Table 5: Association between Prothrombin time and severity of covid 19 infection

Severity	Mean (sec)	SD	P value
Mild	30.49	9.17	0.78
Moderate	36.47	9.29	
Severe	36.98	8.60	

Table 6: Association between activated partial thromboplastin time and severity of covid 19 infection

Severity	Mean mg/dl	SD	P value
Mild	438	1.15	0.65
Moderate	493	1.26	
Severe	440	2.07	

Table 7: Association between fibrinogen and severity of covid 19 infection