



D-dimer parameters in COVID-19 (Prospective study in 100 patients)

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ABSTRACT

A new virus called the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was identified as the cause of a disease outbreak that began in China in 2019. The disease is called coronavirus disease 2019 (COVID-19).

Methods One hundred covid-19 cases were verified by RT PCR in a multi-center, prospective, observational and interventional investigation. At admission, HRCT of the chest, oxygen levels, and the inflammatory marker D-Dimer were all measured in all instances. the main focus and the subsequent discussion. Lung fibrosis and its presence or absence were noted together with age, gender, comorbidities, BIPAP/NIV usage, and outcome. Using CT pulmonary angiography and lower limb venous doppler, doctors can rule out DVT and PTE in some patients. The Chi-square test is used for statistical analysis.

Results: There is a strong link between the severity score obtained on the first CT and the D-dimer level.[p<0.00001] The length of sickness before admission is significantly correlated with D-Dimer levels.[p<0.00001] D-Dimer levels are significantly correlated with the presence of comorbidities. [p<0.00001] There is a strong correlation between oxygen saturation and D-dimer levels.[p<0.00001]

The need for BIPAP/NIV is significantly correlated with D-Dimer concentration.[p<0.00001] D-Dimer concentration is significantly correlated with the timing of BIPAP/NIV need while hospitalized.[p<0.00001] Post-covid lung fibrosis, deep vein thrombosis, and pulmonary thromboembolism are significantly associated with the D-Dimer titer during hospitalization during follow-up compared to normal and abnormal to entrance point level.[p<0.00001].conclusion. D-Dimer's proven highly essential function in predicting sickness severity and measuring responsiveness to therapy during hospitalization in covid-19 pneumonia has led researchers to this

Aims: The effects of Covid-19 pneumonia on the lung parenchyma, airways, and vasculature are diverse since this illness is heterogeneous.

Keywords:

Inflammatory marker, deep vein thrombosis, pulmonary embolism, lung fibrosis, Covid-19 pneumonia, and other forms of pneumonia

Introduction

Covid 19

Epidemiology

Since the first reports of cases from Wuhan, at the end of 2019, more than 80,000 COVID-19 cases have been reported in China; including all

laboratory-confirmed cases as well as clinically diagnosed cases in the Hubei Province. Increasing numbers of cases have also been reported in other countries across all continents except Antarctica. The rate of new cases outside of China has outpaced the rate in China which

led world health organization (WHO) to declare COVID-19 as a pandemic.

Incubation period

The exact incubation period is not known. It is presumed to be between 2 to 14 days after exposure, with most cases occurring within 5 days after exposure [8, 9, and 10].

The spectrum of illness severity

Most infections are self limiting. COVID-19 tends to cause more severe illness in elderly population or in patients with underlying medical problems. As per the report from Chinese center for disease control and prevention that included approximately 44,500 confirmed Infections with an estimation of disease severity

- Mild illness was reported in 81% patients
- Severe illness (Hypoxemia, >50% lung involvement on imaging within 24 to 48 hours) in 14%
- Critical Disease (Respiratory failure, shock, multi-organ dysfunction syndrome) was reported in 5 percent
- Overall case fatality rate was between 2.3 to 5%

1. Age affected

- Mostly middle aged (>30 years) and elderly.
- Affects pregnant women
- Symptomatic infection in children appears to be uncommon, and when it occurs, it is usually mild

2. Clinical Presentation

In a study describing 1099 patients with COVID-19 pneumonia in Wuhan, the most common clinical features at the onset of illness were

- Fever in 88%
 - Fatigue in 38%
 - Dry cough in 67%
 - Myalgias in 14.9%
 - Dyspnea in 18.7%
- .Pneumonia appears to be the most common and severe manifestation of infection. In this group of patients breathing difficulty developed after a median of five days of illness. Acute respiratory distress syndrome developed in 3.4% of patients.

3. Other symptoms

- Headache
- Sore throat
- Rhinorrhea
- Gastrointestinal symptoms

About 80% of confirmed COVID-19 cases suffer from only mild to moderate disease and nearly 13% have severe disease (dyspnea, respiratory frequency ≥ 30 /minute, blood oxygen saturation $\leq 93\%$, PaO₂/FiO₂ ratio < 300 , and/or lung infiltrates $> 50\%$ of the lung field within 24-48 hours).

Critical illness (respiratory failure, septic shock, and/or multiple organ dysfunction/failure) is noted in only in less than 6% of cases.

4. D-dimer

is one of the protein fragments produced when a blood clot gets dissolved in the body. It is normally undetectable or detectable at a very low level unless the body is forming and breaking down blood clots. Then, its level in the blood can significantly rise. This test detects D-dimer in the blood.

When a blood vessel or tissue is injured and begins to bleed, a process called hemostasis is initiated by the body to create a blood clot to limit and eventually stop the bleeding. This process produces threads of a protein called fibrin, which cross-link together to form a fibrin net. That net, together with platelets, helps hold the forming blood clot in place at the site of the injury until it heals.

Once the area has had time to heal and the clot is no longer needed, the body uses an enzyme called plasmin to break the clot (thrombus) into small pieces so that it can be removed. The fragments of the disintegrating fibrin in the clot are called fibrin degradation products (FDP), which consist of variously sized pieces of crosslinked fibrin. One of the final FDP produced is D-dimer, which can be measured in a blood sample when present. The level of D-dimer in the blood can significantly rise when there is serious formation and breakdown of fibrin clots in the body.

D-dimer parameters in covid 19

1 Association between Levels of D-Dimer and COVID-19 As stated above, the levels of D-dimer directly correlate with the rate of formation and degradation of plasmin. Hence, any pathological condition that upregulates the rate of plasmin generation and degradation would also increase the levels of D-dimer. Thus, the pathologies that promote chronic inflammation, such as rheumatoid arthritis, asthma, and cancer, also lead to an increase in

the levels of D-dimer. It follows that infection of a novel coronavirus, which leads to upregulated inflammatory reactions among individuals, would also increase the levels of D-dimer.

This is evident by the findings of several previous studies that showed that levels of D-dimer were significantly higher in COVID-19 patients, especially those who were either severely ill or had deceased. Some investigators have postulated that the upregulated levels of D-dimer in individuals with severe novel coronavirus infection might be associated with severe illness, higher rates of thrombotic activity, and higher mortality rates of such patients. In 2020, Guan et al. presented the results of a large retrospective study that indicated the correlation between abnormal levels of D-dimer and disease severity of the COVID-19 patients for the first time. Setting a cut-off point of a D-dimer level of more than 0.5 mg/L, they reported that a significantly higher proportion of novel coronavirus infected individuals with severe illness exhibited abnormally high levels of D-dimer than those with only mild or moderate illness ($p=0.002$). Furthermore, Tang et al. reported that COVID-19 patients with a severe level of illness exhibited approximately 3.5 times higher levels of D-dimer compared to patients with only mild or moderate levels of illness. Their results were corroborated by Wang et al., who reported approximately 2.5- and 5-times higher levels of D-dimer, respectively, in COVID-19 patients with a severe level of illness compared to patients with only mild or moderate levels of illness.

In line with these findings, Wang et al. also found that the levels of D-dimer in COVID-19 patients with severe illness were more than two times lower compared to the levels of D-dimer of deceased COVID-19 patients. Their results were supported by Tang et al., who demonstrated that COVID-19 patients with severe illness exhibited around four- and nine-times lower levels of D-dimer, respectively, compared to the levels of D-dimer of deceased COVID-19 patients.

2. Covid-19 and Thrombosis Since its emergence, several investigators around the globe have published a plethora of studies on the epidemiology of COVID-19. Although its

transmittance rate is extremely high, it has a very low mortality rate of 2.3%

A higher incidence of COVID-19 has been reported among individuals aged more than 65 years and less than 18 years, with a higher sequential organ failure assessment (SOFA) score, male gender, and several comorbidities, including diabetes, hypertension, and coronary heart disease.

In addition, several studies have also shown that a D-dimer level of more than $1 \mu\text{g/mL}$ to be a potential risk factor of COVID-19.

The formation of thrombi has been reported in both the venules as well as the arterioles of COVID-19 patients at the time of hospitalization. It has been postulated that this observation could be attributed to the risk factors that contributed to the aggravation of COVID-19 in an individual, such as obesity, pregnancy, and comorbidities like diabetes mellitus, which often themselves participate in and trigger the formation of clots in the bloodstream.

The formation of such thrombi and the resultant angiogenesis often give rise to impaired microcirculation in COVID-19 patients.

Previous studies on COVID-19 patients have shown that the novel coronavirus is often responsible for endothelial injury and cell membrane destruction. This, in turn, reduces the fibrinolytic activity of endothelial cells, which promotes the formation of thrombi. It is noteworthy that the proinflammatory cytokines are involved in both inflammatory and coagulatory processes. Previous studies have shown that severe infection of novel coronavirus triggers severe inflammatory reactions, as indicated by the significant upregulation of proinflammatory cytokines. The cytokine upregulation and coagulopathy observed in cases of severe novel coronavirus infection have been attributed to acute sepsis. Furthermore, severe novel coronavirus infection often predisposes infected individuals to sepsis-induced coagulopathy and disseminated intravascular coagulation. Recently, Maier et al. reported a significant association between novel coronavirus infection and an increase in the viscosity of the plasma of the infected individual. Such an increase in plasma viscosity has been reported to be associated with an increase in SOFA scores. This finding indicated that

hyperviscosity of the plasma could trigger both endothelial dysfunction as well as thrombosis. Blood viscosity is also affected by fibrinogen levels. Previously, it has been reported that the fluidic state of the plasma is maintained only till thrombin is able to cleave about 25% to 30% of the plasma fibrinogen. This, in turn, facilitates efficient polymerization of fibrin monomers and promotes the activation of plasma factor XIII by thrombin. It is demonstrated that COVID-19 patients also exhibited high plasma levels of fibrinogen.

D-dimers, as degradation products of fibrin, are widely used in the diagnosis (exclusion) of venous thrombosis. In addition, D-dimers have been shown to be of prognostic value in various diseases, including cancer and cardiovascular disease. There is plethora of data on the coagulation disturbances in patients with COVID-19, both clinically and by the use of various laboratory measurements. D-dimers in predicting the severity of COVID-19. A high D-dimer at admission was an independent predictor for mortality in COVID-19 patients from Wuhan. Patients with a D-dimer ≥ 2.0 mg/ml had a much higher mortality incidence than those with levels < 2.0 mg/ml (HR 51.5),¹ where the HR was 18.4 in D-dimers ≥ 1.0 mg/ml.² Also, D-dimers were able to distinguish patients with moderate from severe disease in 75 patients from China.³ Even more so, dynamic changes of D-dimer levels during the course of the disease was prognostic of poor outcome in 276 Chinese patients.⁴ D-dimers in predicting the occurrence of pulmonary embolism in patients with COVID-19. Higher D-dimer levels were associated with a greater probability of pulmonary embolism 3, 6, 9, and 12 days after determining D-dimer levels with an OR of 1.7, 2.0, 2.4, and 2.4, respectively in 21 patients from Spain.⁵ Similar results were found in 106 French patients, although the D-dimer threshold to exclude PE (2660 mg/L) was much higher than usual.⁶ A higher threshold was also suggested in 156 COVID-19 patients with asymptomatic deep venous thrombosis.⁷ D-dimers to guide anticoagulation. Anticoagulation therapy was associated with lower mortality in COVID-19 and this was especially true for patients with high D-dimers.⁸ As the relationship between D-dimers and the severity of COVID-19 and/or the

occurrence of PE is evident and even appears to be dynamic, it is appealing to start an early intervention based on D-dimer levels. Several clinical guideline already advocate the use of different D-dimer cut-off levels to determine the anticoagulation dose. However, as a recent review pointed out very clearly,⁹ there is a high variety of D-dimer tests with a large variability in the way they report their results. Most importantly, differences in the reported units (either D-Dimer Units [DDU]) or Fibrin Equivalent Units [FEU], the assay cut-off values and the absolute measuring units (mg/L, ng/mL, m/mL) hamper generalisability of the results and the use of a clear cut-off point for decision making. The authors correctly call out for at least fully reporting the necessary variables to ensure study results can be translated to other clinics. Therefore, although the role of D-dimers in guiding treatment of COVID-19 is attractive, clinicians should be aware of the details of their local D-dimer test before implementing standard cut-offs provided by others.

Main Points

- **Some demographic data including age and gender were considered as the most essential factors in predicting patients' survival.**
- **The proposed cut-off for D-dimer in predicting patient outcome was 1.49 mg/L**
- **The use of D-dimer as a predictive measurement of patient death has 82.69% sensitivity and 68.09% specificity.**
- **Higher D-dimer (> 1.49 mg/L) was associated with a lower 30-day survival rate than the lower D-dimer groups (8 days difference).**
- **D-dimer was the second-best laboratory marker for the mortality prediction of coronavirus disease 2019 patients.**

CTPA image acquisition

CTPA examination were performed in multi-detector CT scan (Philips Ingenuity Flex 32, Philips Medical Systems, Best, the Netherlands)

by using a standard CTPA protocol. All patients were instructed to hold breath to minimize motion artifacts. The whole chest was scanned from lowest hemidiaphragm to the lung apex for each patient in the supine position. The tube voltage of 120 kV, tube current of 314 mA, collimation of 64x0.625mm, pitch of 0.937- 1, table speed of 65mm / s, gantry rotation time of 0.75s. 80-100 mL nonionic iodinated contrast media (Iomeprol, Iomeron 300 Bracco, Milan, Italy) was injected into an antecubital vein at a

flow rate of 4mL / s followed by a 25mL saline flush using a mechanical power injector. We used the automatic bolus tracking technique with a trigger threshold of 150 HU, and a fixed delay of 4s for optimal intraluminal contrast enhancement. The images were reconstructed with a thickness of 1-2mm. Finally the images were transmitted to post-processing workstations for multiplanar reconstruction and picture archiving and communication systems (PACS).

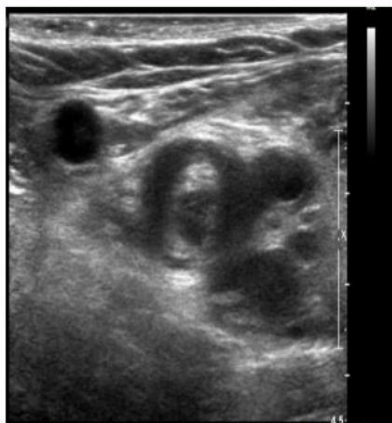


Figure 4. Ultrasound of the right lower limb in a 66 year old woman, who was diagnosed with COVID-19. The image shows soft intraluminal material and a non-compressible venous segment of the femoral vein as signs of acute deep vein thrombosis.



Figure 1. Images in a 61 year old man with COVID-19 pneumonia. A, axial chest CT in lung window obtained on day 10 after the onset of symptoms shows areas of peripheral ground-glass opacities (black arrow). B, axial CT pulmonary angiography demonstrates bilateral filling defects (white arrows) involving main pulmonary arteries.

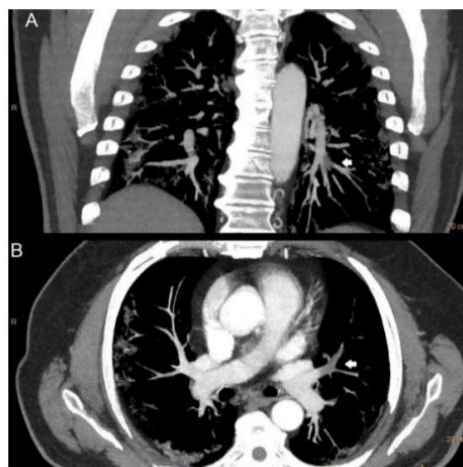


Figure 3. Images in a 65 year old man with COVID-19 pneumonia. A, coronal thick maximum intensity projection slab of CT pulmonary angiography demonstrates a filling defect (white arrow) in a segmental artery for the left lower lobe. B, axial thick maximum intensity projection slab of CT pulmonary angiography shows another filling defect (white arrow) involving lingular artery.

High D-Dimer Levels May Be Predictive of a Poor Patient Outcome

The D-dimer levels of 169 COVID-19 patients on admission were ≤ 1.49 mg/L, and 118 patients had D-dimer levels greater than 1.49 mg/L, according to the cut-off value. There were 52 non-survivors, with 43 having D-dimer levels > 1.49 mg/L and the rest having D-dimer levels of ≤ 1.49 mg/L. Male patients had a lower cut-off for D-dimer in comparison with female patients (> 1.49 mg/L vs. > 2.2 mg/L). The sex and comorbidities-adjusted survival curve between

the patients with D-dimer levels of > 1.49 mg/L and less than or equal to 1.49 mg/L. The unadjusted Kaplan–Meier plot is also provided in Supplementary Figure 1. The ROC curve for D-dimer's predictive role on patient death demonstrated 82.69% sensitivity and 68.09% specificity at the 1.49 mg/L cut-off. This graph's area under curve (AUC) was 0.786 ($P < .001$). Patients with D-dimer levels of > 1.49 mg/L had a significantly higher risk of subsequent mortality ($P < .001$), as shown by the lower 30-day survival rate than patients

with D-dimer levels of 1.49 mg/L, according to Kaplan-Meier curves and were analyzed using the Mantel-Haenszel log-rank test. The difference in average survival time between these groups is about 8 days (29 vs. 21 days). During hospitalization, there were 52 death occurrences, 43 of which were observed in patients with D-dimer levels of >1.49 mg/L on admission, while only 9 in those with lower D-dimer levels (HR = 8.72,

95% CI: 4.24-17.93, $P < .001$). After the multivariable analysis, only the D-dimer, sex, and coexisting disorders were found to be significant determinants for the risk of COVID-19 mortality. The adjusted HR value was provided in value of the C-index to predict in-hospital mortality in COVID-19 patients among regularly observed laboratory tests

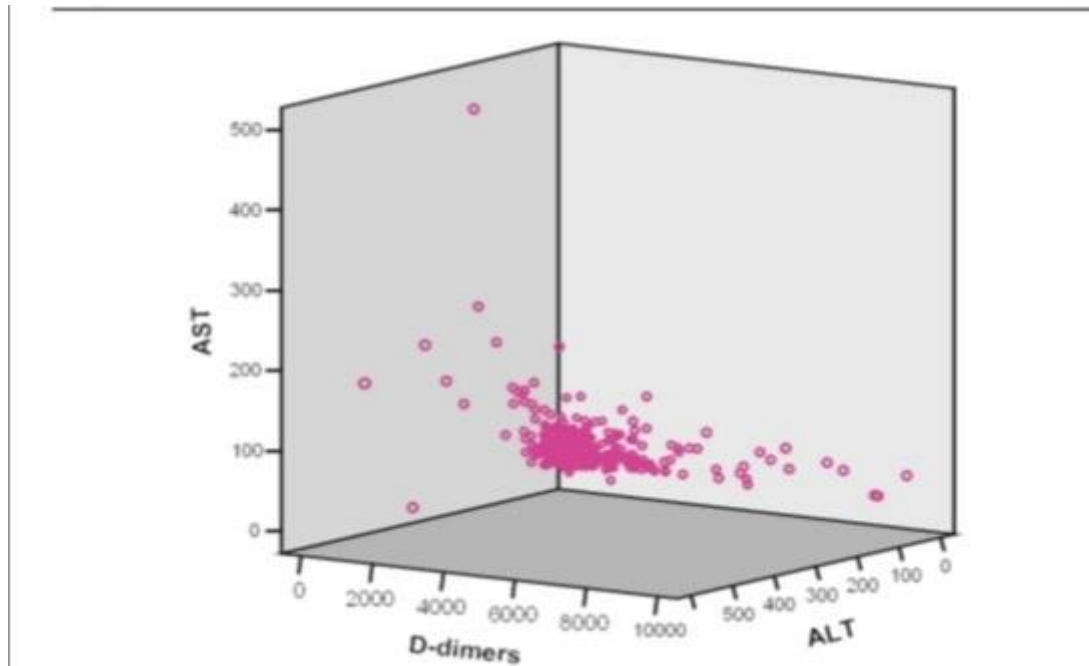


Figure 2 The correlation between the D-dimers, ALT and AST values at the beginning of hospitalization of patients.

Patients And Methods

During the time period of February 2020 - February 2021, a multi-center, prospective, observational research was carried out.

Included

To determine the effect of D-Dimer in predicting the severity of disease, measuring responsiveness to therapy, and prognosis as post-covid fibrosis and DVT/PTE in patients with covid-19 pneumonia admitted to the intensive care unit, the study comprised one hundred cases verified by RT PCR. Following Institutional Review Board (IRB) permission and patient written informed consent, a total of 100 patients were recruited in the research.

Criteria for inclusion: Patients with Covid-19, as verified by RT-PCR, who were 18 years or older, hospitalized at study centers (regardless of severity or oxygen saturation) were enrolled.

Criteria for exclusion: Participants who were unable to provide informed permission, who had abnormal D-dimer results, or who declined further follow-up were not included.

Prior to study enrollment, all patients were evaluated using the following criteria:

If the first RT PCR test for Covid-19 was negative despite strong radiographic evidence of pneumonia, we retested all patients and included only those with a positive result.

2. A high-resolution computed tomography (HRCT) of the chest is used to determine the degree to which the lungs are affected.

Third, the clinician will record vital signs such as the patient's pulse, respiration rate, blood pressure, and the presence or absence of any unexpected breathing noises.

Complete blood count, liver function, blood sugar, kidney function, electrocardiogram

5. Initial and periodic evaluation of viral inflammatory markers (D-Dimer, C-Reactive Protein, and Interleukin-6) during the course of disease. Parameter values were categorized as normal or abnormal based on the criteria used in pathology laboratories.

Clinical factors and the first D-dimer titer were used to determine the degree of disease.

If a normal D-Dimer test was performed at admission, a second test was performed on the day of release or if the patient's condition worsened while in the hospital.

The severity, course of illness, and titer level used to evaluate response to medical therapy were evaluated during follow-up visits every 72 hours if D-Dimer assay was abnormal at entrance point.

Lower limb venous doppler for DVT and/or CT pulmonary angiography for pulmonary thromboembolism should be performed in select instances with abnormal D-dimer or persistent tachycardia.

Evaluation of D-Dimer Titers:

Consistent norms: Consistent norms 70-470 mg/dL

Results interpretation:

D-dimer values up to 470 ng/mL are considered normal. Values over 470 mg/dL are considered positive. D-Dimer levels increased significantly (by a factor of 2) Significantly, the D-Dimer level increased by a factor of 4.5. Values that increase or decrease by a factor of two to four in the follow-up are statistically significant. The chi-squared test was used for the statistical analysis. The probability table showed that there were a number of significant 2 values for varying degrees of freedom. A p-value of less than 0.05 was deemed statistically significant,

while a p-value of less than 0.001 was deemed very so.

Analysis and observations:

One hundred cases of pneumonia caused by covid-19 were verified by covid-19 RT PCR; of these, 65 were male and 35 were female; 600 were older than 50 years old, and 400 were younger than that age. There is a strong association between CT entrance severity score and D-dimer levels in instances with covid-19 pneumonia. [p<0.00001] .In instances of pneumonia caused by the covid-19 virus, the higher the D-Dimer level, the longer the patient will be sick. [p<0.00001] (Table 2). Variables such as age, sex, diabetes mellitus, ischemic heart disease, high blood pressure, chronic obstructive pulmonary disease, and obesity have been shown to have a significant impact on D-Dimer and COVID-19 pneumonia. [p<0.00001]. In instances with covid-19 pneumonia, the D-Dimer level is significantly correlated with oxygen saturation. [p<0.00001].

Statistical analysis

Descriptive analysis were used to characterize the study sample by demographics, including sex, age, prevalence of hypertension, stroke, heart disease in relation to anemia and kidney function. The result was presented in the form of tables, using frequencies percentage, mean and standard deviation to describe the study sample in relation to relevant variables. P-value less than 0.05 was taken as statistical significant. Chi-square statistics was used for testing the association between the categorical variables. All the data were manually checked for its clarity and completeness, then coded, entered and transported to IBM SPSS version 22.0 software package for analysis.

Results

Table 1. Duration of illness (Doi) at entry point during hospitalization and D-Dimer level in covid-19 pneumonia cases (n=100)

| Duration of illness | Normal D-Dimer (n=32) | Abnormal D-Dimer (n=68) | Analysis |
|---------------------|-----------------------|-------------------------|------------------------------------|
| <7 days (n=34) | 3 | 31 | Chi test value 185.65 p<0.00001 |
| 8-15 days (n=46) | 16 | 30 | |
| >15 days (n=20) | 13 | 7 | |

Table 2. Other variables and D-Dimer level in Covid-19 Pneumonia cases (n=1000)

| COVID-19 RT PCR positive (n=100) | Normal D-Dimer (n=32) | Abnormal D-Dimer (n=68) | Chi test value and P value |
|----------------------------------|-----------------------|-------------------------|----------------------------|
| Age >50 years | 14 | 46 | $\chi^2=51.75$ |
| Age <50 years | 18 | 22 | $p<0.00001$ |
| Male gender | 19 | 46 | $\chi^2=6.6$ |
| Female gender | 13 | 22 | $p<0.010$ |
| Diabetes mellitus | 15 | 45 | $\chi^2=33.74$ |
| Without diabetes | 17 | 23 | $p<0.00001$ |
| Hypertension | 16 | 5 | $\chi^2=238.56$ |
| Without Hypertension | 16 | 63 | $p<0.00001$ |
| COPD | 10 | 5 | $\chi^2=97.44$ |
| Without COPD | 22 | | $p<0.00001$ |
| IHD | 11 | 63 | $\chi^2=60.74$ |
| Without IHD | 21 | 9 | $p<0.00001$ |
| obesity | 2 | 59 | $\chi^2=33.29$ |
| Without obesity | 30 | 14 | $p<0.00001$ |

Table 3 .Oxygen saturation at entry point and D-Dimer level in Covid-19 pneumonia cases (n=100)

| Oxygen saturation | Normal D-Dimer (n=32) | Abnormal D-Dimer (n=68) | Analysis Chi test value |
|-------------------|-----------------------|-------------------------|-------------------------|
| >90% (n=21) | 10 | 10 | 60.37 $p<0.00001$ |
| 75-90% (n=49) | 15 | 34 | |
| <75% (n=30) | 6 | 24 | |

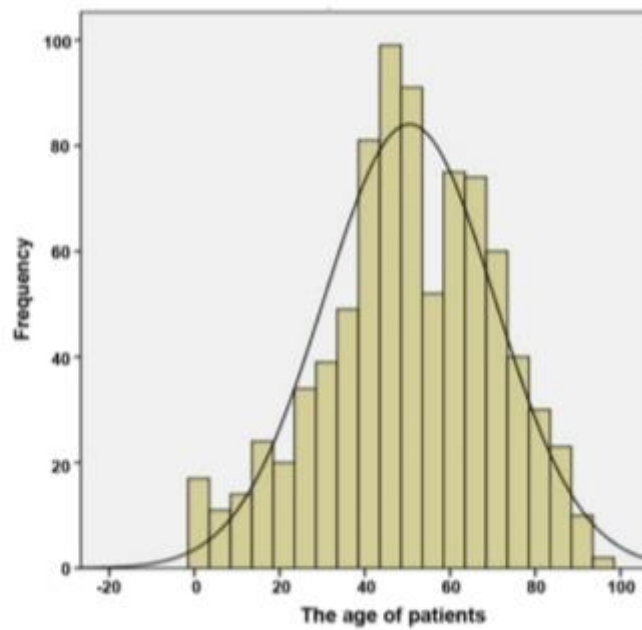


Figure 1 Distribution by age, total group of patients.

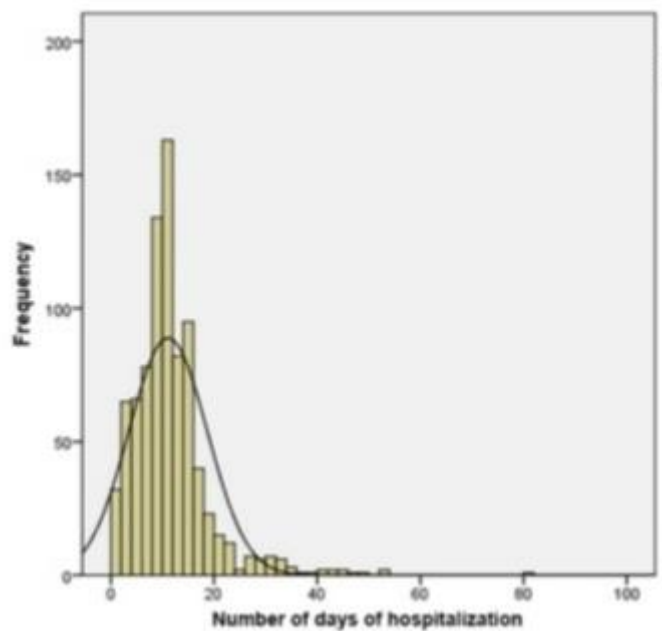


Figure 2 Distribution according to the hospitalization duration of the total patients group

Discussion

D-dimer is a protein fragment that is created when a blood clot is disintegrated. D-dimer levels over normal are a common indicator of thrombotic events including DVT, PE, or DIC (disseminated intravascular coagulation), which can be fatal if left untreated.

Increased D-dimer levels have been linked to more advanced disease and poorer outcomes in COVID-19 patients. Although the specific processes linking the virus to an increased risk

of thrombotic events remain unknown, it is believed that the virus either directly or indirectly promotes the production of blood clots. D-dimer levels can be measured clinically to help identify COVID-19 individuals at high risk for thrombotic problems. Several prognostic scoring systems have been developed to help identify patients at higher risk of mortality or ICU admission when dealing with COVID-19. One such system is the D-dimer adjusted International Severe Acute

Respiratory and Emerging Infection Consortium (ISARIC) Clinical Characterisation Protocol. D-dimer levels are often high during pregnancy, but they can also be elevated after cancer treatment, surgery, trauma, or liver illness. Therefore, D-dimer values must be interpreted in the context of the full clinical picture.

D-dimer is a helpful biomarker for the detection of thrombotic disorders because it is a byproduct of fibrinolytic breakdown of fibrin and because it indicates the presence of a hypercoagulable state and secondary fibrinolysis in the body when levels are increased. Hypercoagulability has been recorded among COVID-19 patients(10); whereas 71% of COVID-19-related deaths were determined to meet the DIC criterion, this ratio was just 0.6% among survivors(5). In addition, 30% of COVID-19 patients were diagnosed with pulmonary embolism, and the incidence of venous thromboembolism (VTE) was 25% in patients with severe COVID-19(6,11).

From a total of 231, 84 (36.6%) patients were found to have an abnormal D-dimer level. This research has a strong p-value since it covered both patients under home surveillance and outpatients with minor symptoms. Using real-time reverse transcription-polymerase chain reaction (PCR), patients in this research ranged in age from 14 to 75 years old, with a mean of 44.5 years.

It has been reported that fatal outcomes from COVID-19 are accompanied by cytokine storm syndrome and ferritin level was significant in COVID-19 home observation patients(12), many studies were conducted on severe and very severe COVID-19 hospitalized patients, and many of these patients died. It appears that coagulopathy and overt disseminated intravascular coagulation have a substantial risk of death. D-dimer elevation was the most significant independent predictor of death among the coagulation markers in a study of 191 patients. High levels of D-dimer have been found in 91 of the 183 people who did not make it (8), and a study of 183 cases found that 21 of the non-survivors had considerably longer prothrombin and activated partial thromboplastin durations than the survivors did (5). Study after study has shown that D-dimer levels are elevated in severe cases; for example, Han et al. reported an increase in D-

dimer levels compared to controls in 94 cases(13), Wu et al. reported an increase in D-dimer levels in ARDS cases(14), Zhang et al. studied 140 cases and found an elevation of D-dimer in severe cases(15), Gao et al. examined 43 cases (28 mild and 15 severe

Conclusion

- Corona virus disease 2019 (COVID-19) was reported as cluster of disease in China in December 2019
- It has since spread to all continents except Antarctica and WHO declared COVID-19 as a pandemic.
- Elderly persons with co-morbidities are more affected
- In conclusion, it is clearly evident that levels of D-dimer are directly associated with the disease severity among COVID-19 patients.
- Novel coronavirus infections promote inflammatory and coagulation reactions, leading to an increase in thrombotic event rates.
- Currently, the evaluation of levels of D-dimer has not been adopted in the routine laboratory assessment of COVID-19 patients.
- Laboratory testing for D-dimer and proinflammatory cytokines could help to categorize the COVID-19 patients based on the severity of their illness.
- This could, in turn, be helpful in adequate and more efficient management of such individuals.

Recommendations

The test shows the presence of clots in the body when COVID becomes serious. We get a lot of clots in the body in the lung especially, because of which reason the lungs cannot breathe. The blood flow is hampered due to clotting. So, the body tries to break down these clots. D dimer is detectable for up to eight hours after formation until the time the kidney clears it out.

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