



Research Paper

SIGNIFICANCE OF ANTICOAGULANTS IN COVID-19

Ananth Krishna , Risav Banerjee and Mohammed Mansoor Zarian

Department of Biochemistry,
Indian Academy Degree College – Autonomous,
Hennur road, Bengaluru – 560043,
India.

Abstract

We aim to provide a comprehensive study of the significance of anticoagulants in the COVID-19 patients. As the COVID-19 patients have been found that they suffer with thromboembolic diseases, elevation of the D-dimer and LDH (lactose dehydrogenase) levels. It has been found that the thrombotic disease in the COVID-19 patients has been increased by 31%. It is a major reason for the high number of mortality rates among the COVID-19 patients.

BACKGROUND

Acute respiratory disease which is commonly termed as novel coronavirus, which is caused by a RNA virus SARS-CoV-2. Which caused a global pandemic. It has a high mortality mostly with the patients having comorbidities.

It has spread from Wuhan, China which is having more than 6.4 billion cases and 34lakh deaths worldwide.

Although the most of the patients with the coronavirus disease 2019 which is commonly known as (Covid-19) have a respiratory tract infection which mostly results into pneumonia. The infection caused by this coronavirus varies from asymptomatic mild symptoms and severely affected patients. Patients with the COVID-19 faces mild to high fever, cough, fatigue and shortness of breath. Recent findings have also stated that patients are also having abdominal pain and diarrhea.

Data shows that 20% of the symptomatic patients requires hospitalization and intensive care unit (ICU) and 12% needs ventilator support.

The mortality rate of the COVID-19 is lower than that of SARS and Middle East Respiratory Syndrome (MERS). The severity rate is higher in the comorbid patients with diabetes mellitus, hypertension or obesity.

SARS-CoV-2 invades the host cell by binding it to the receptor through its spike protein which is angiotensin converting enzyme 2 (ACE2).

Many patients with COVID-19 have coagulation abnormalities which is associated with severe infections like disseminated intravascular coagulation (DIC) or thrombotic microangiopathy. The coagulation abnormalities have increased the mortality rate among the COVID-19 patients.

Extensive thrombosis in the small vessels and the microvascular in lungs and extrapulmonary organs have been confirmed histologically (Zhang, et al 2020). The rate of venous thromboembolism in the hospitalized patients can be high as 25% and it can expand to other macrovascular thrombotic complication such as higher than expected prevalence of pulmonary emboli in patients with COVID-19 (Klok, et al 2020, Stoneham, et al).

The coagulation abnormalities are characterized by elevated D-dimer level with normal platelet count and normal/elevated fibrinogen level.

D-dimer level greater than 1 μ g/ml is associated with a poorer prognosis.

Patients requiring with mechanical ventilation who were treated with therapeutic anticoagulation had an inhospitality mortality of 29.1% compared to 62.7% in patients who did not receive anticoagulation.

Longer duration of anticoagulation was associated with a reduced risk of mortality (Paranjpe, et al 2020).

In a recent study from China where a series of 1099 patients with elevated D-dimer levels (>0.5 mg/L) was found in 260 (46%) of 560 patients.

In other study it was seen that 183 patients with COVID-19 in China, a mean D-dimer concentration of 2.12mg/L (range 0.77 – 5.27) in survivors. In another study found that patients who were admitted to the intensive care unit (ICU) had significantly higher median D-dimer concentration (2.4 mg/L, IQR 0.6-14.4) than patients who received no ICU care (0.5 mg/L, 0.3-0.8).

The hospitalized COVID-19 patients were treated with antithrombotic agents for protection against venous thromboembolism.

In a study it was found that elevated D-dimer levels is associated with higher 28day mortality rate, while the patients with higher platelet count was associated with lower 28-day mortality patients. It has been found that the patients with thromboembolism suffer with gangrene.

From a study of Wuhan, China it was reported that the VTE (venous thromboembolism) in COVID-19, the patients those who were admitted in the ICU was 25%. A profound study from the Netherlands it was found that a higher incidence of thromboembolic patients i.e., 31% was found despite the use of standard weight based VTE prophylaxis. The thrombotic events include pulmonary embolism, deep venous thrombosis, ischemic stroke, myocardial infraction.

In a study high number of patients were found to have pulmonary embolism. The ischemic stroke and myocardial infarction were reported in the younger patients suffering from COVID-19.

DISCUSSION

It has been well established that the virus named Covid 19 targets the respiratory system, which ultimately leads to failure of the lungs to harvest the necessary amount of oxygen from the air in order to supply the body's need. However, several recent studies have shown that Covid 19 can be directly or indirectly affect the heart, skin, kidneys, and be the cause of many coagulation related diseases such as disseminated intravascular, hypercoagulability etc. The primary reason for such abnormalities is suspected to be the increase in concentration of the D-dimer (which can result in thrombosis). The proof of this cause is given by multiple scenarios and patterns emerging in infected individuals. An example of few such studies can be a case study done in China. In this case study around 1099 patients from 522 hospitals were reviewed and it was found out that the D-dimer is more elevated in critically ill patients (65/109,59.6%) when compared to patients who had a less severe version of the disease (195/451,43.2%). This study also showed a decrease in platelet concentration and increase in antiphospholipid antibodies, which were further backed by studies from other parts of the world. In addition to increase in concentration of the D-dimer other reasons such as increase in levels of Lactate dehydrogenase, bilirubin, decrease in the number of platelets; microangiopathies were made known in an article written by Campbell. In a case study conducted by the New England Journal of medicine, where it was found out that severe cases of infection of the Covid !9 virus had been tested

positive for anticardiolipin anti-IgA, anti-B2 glycoprotein IgA and IgG which could be caused by APS (antiphospholipid syndrome). Upon activation these molecules can cause endothelial cell damage. Such coagulative abnormalities can cause major damage to the blood vessels and the heart. Acute respiratory symptoms can be associated with cardiovascular deaths especially in older individuals and also individuals with preexisting cardiovascular diseases. A recent study showed that capillary thrombosis which can be characterized by thickened alveolar capillaries with surrounding edema and thrombi in the bed of the capillaries and small vessels caused development of pulmonary artery hypertension and heart failure due to development of thrombosis in the lungs. The results may be stroke in young patients up to 33 years old which was investigated in a case study where 5 people around this age who were infected with Covid 19 died due to stroke. Inflammation induced thrombosis is a well understood part of the immune system to respond to infections or trauma. Macrophages together with leucocytes recruited by C3a and C5a to the site of infection are responsible for releasing pro inflammatory cytokines such as IL-1, IL-2R, IL-6 and IL-8. These factors cause tissue damage and inflammation in the nearby tissue. Due to this interstitial inflammation was widely seen in patients who died due to the virus. Antithrombin-432 amino acid serpin produced by the liver is one of the most powerful anticoagulants recognized. It works antagonistic to thrombin and factor x (responsible for clotting). A pooled analysis performed on Covid 19 patients calculating the weighted mean difference along with 95% confidence interval. In this studies Antithrombin values were lower in Covid-19 patients with severe illness. The difference from normal values ranged from -4 to 25 iu/dl. But the studies regarding this topic were very limited providing very less and unreliable data. It was recommended to Covid patients whose D-dimer levels were above the 4 times of normal to be administered with a subcutaneous dose of 100IU/KG of low molecular weight heparin (LMWH) per day. This prescription is for high thrombic risk patients. For low thrombic risk patients 1 mg/kg was recommended. A new method of detecting sepsis induced disseminated intravascular coagulation proposed by the International society of Thrombosis and Haematosi s was called sepsis induced coagulopathy in this study of 499 patients with severe Covid-19 infection 99 were treated with LMWH for 7 or more days. It was found out that 28 mortality day of heparin users was lower than non-users for Covid 19 patients with D-dimer >3ug/ml.

They also had an increased platelet count. LMWH on the onset of ARDS reduces the risk of 7-day mortality by 48%- and 28-day mortality by 37%.

CONCLUSION

Covid 19 or SARS CoV-2 during an infection increases the chances of blood clots in patients due to elevated d dimer levels which is due to the body mounting an immune response to the virus. There is also an increase in thrombin levels of blood which further increases the likelihood of coagulating disorders, which can be life threatening. An available solution to this would be anticoagulant therapy or thrombolytic therapies along with immunomodulatory therapy which may ease the stress on the body due to infection and help with maintaining a degree of homeostatic conditions in the blood. Further research in this field may help us better understand the reactionary affect of the human body to this new strain of virus.

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