

The changes of Coagulation State in Patients Contracted with SARS-COV-19

Anahita Nosrati^{1,2*} 

1. Iranian Journal of Pathology Editorial Board
2. Department of Pathology, Imam Hospital, Mazandaran University of Medical Sciences, Sari, Iran

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Corresponding Information:

Anahita Nosrati; Department of Pathology, Imam Hospital, Mazandaran University of Medical Sciences, Sari, Iran. Email: anahita785@gmail.com

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Coronaviruses are considered to be one of the most significant human and animal pathogens. In late 2019, a new species of coronavirus was recognized as the cause of some pneumonia cases in Wuhan, China.

The disease spread rapidly and made an epidemic in China and subsequently in almost all countries in the world. In February 2020, the World Health Organization (WHO) named it as COVID-19 standing for Coronavirus 2019 (1).

Due to being a pandemic issue, it is needed to discuss various aspects of this viral disease. Recently, Yan Zhang *et al.* reported a case of coagulopathy and antiphospholipid antibodies in the patient with severe COVID-19 infection (2). Thus, one of the serious complications of COVID-19 that should be taken into consideration is coagulopathy with possible antiphospholipid antibodies syndrome in these patients.

In this regard, some studies also claimed that COVID-19 could cause venous and arterial thromboembolism because of excessive inflammation, hypoxia, immobility, and diffuse intravascular coagulation (3). Antiphospholipid syndrome is a systemic autoimmune disease with vascular and hematologic complications as venous and arterial thrombosis or pregnancy morbidity (4).

It is well known that infectious agents are one of the major stimulators of the antiphospholipid antibodies in vivo (5), thus, COVID-19 can be a possible cause of this phenomenon within its infection period and consequently, positive results of antiphospholipid antibodies detection are not unexpected.

1. When does SARS-CoV-2 seroconversion occur? There are different reports for the SARS-CoV-2 infection, varied based on the gender, age, the severity of the disease, and the medical condition background (6).

2. What would be the consequence of antiphospholipid antibody coagulation tests in the patients with COVID-19 infection?

These patients have a prominent hypercoagulable state, with venous thrombotic events (7). Abnormalities have been documented in the coagulation screening tests such as prolonged activated partial-thromboplastin time

(aPTT). This evidence may create a challenge whether the use of anticoagulants could be refused at both therapeutic and prophylactic steps (8).

A prolonged aPTT may come from a clotting factor deficiency or coagulation inhibitors which is either specific (e.g., antibody to factor VIII) or nonspecific (e.g., lupus anticoagulant).

In vitro tests can be affected by Lupus anticoagulant, but typically is not associated with bleeding. Lupus anticoagulant is associated with a thrombotic risk as a part of the antiphospholipid syndrome (7).

One study showed that most patients with COVID-19 infection and prolonged aPTT were also positive for lupus anticoagulant (91%). They were often accompanied by related factor XII deficiency. It is important to note that no observation was related to a bleeding tendency (The factor XII is not required for hemostasis), and also in antiphospholipid syndrome, lupus anticoagulant by itself, may be associated with a thrombotic tendency. Therefore, more studies are needed to resolve the role, if any, of lupus anticoagulant in the pathogenesis of COVID-19 thrombosis (7).

3. Are the unpredicted results of coagulation tests corresponded to the patient's prognosis?

In COVID-19 non-survivors, importantly a higher D-dimer and fibrin degradation product (FDP) levels and besides longer PT are found compared to the survivors at the time of admission.

In this way, the fibrinogen and antithrombin levels are also significantly lower in non-survivors by the late hospitalization. Thus, these evidences suggested that conventional coagulation parameters were importantly associated with the prognosis during the course of COVID-19 infection (8).

4. Is disseminated intravascular coagulation (DIC)- induced death common in the patients with COVID-19 infection?

DIC appears as the most common cause of death. Sepsis associated with organ damage developed in the patients who were diagnosed with virus infection. In all deaths occurring at the end stage, fibrin-related markers (D-dimer and FDP) showed moderate or marked elevation; suggesting a common coagulation activation

and secondary hyperfibrinolysis condition in COVID-19 patients (8). Such data is limited to a relatively small, single-center study; therefore, a more comprehensive clinical study of higher power is needed to confirm those findings. Moreover, some patients have already been hospitalized at the time of manuscript submission.

5. Does prophylactic treatment with anticoagulants affect the prognosis of patients with COVID-19 infection?

Anticoagulant therapy mainly with low molecular weight heparin appeared to be associated with better prognosis in the severe COVID-19 patients meeting DIC criteria or with markedly elevated D-dimer (9).

There were several limitations in those mentioned studies. First of all, a potential selection bias existed in those retrospective studies. Second, severity of the disease and mortality rate of the affected patients might not be representative of the process due to insufficient medical resources at the early stage of the COVID-19 outbreak in Wuhan, China. Third, other therapies which influence those patients have not been evaluated.

It is possible that some non-pharmacological changes have taken place in the management of patients as the doctors learned more about this disease over the period. Nonetheless, this study included a large critical patient population, and due to lack of specific drugs against the infection of SARS-CoV-2 up to now, majority of the patients with severe COVID-19 infection should have received similar supportive treatment after admission. Hence, the results of current study still have certain clinical significance.

The coagulation cascade dysregulation and resultant intra-alveolar or systemic fibrin clots are deleterious evidences in coronavirus infections associated with severe respiratory disease, which have been recognized in both humans and animal models. This is related to the prothrombotic response attempting to preclude diffuse alveolar hemorrhage; otherwise, it can cause overt clot formation with terrible effects on the patient recovery and survival (10).

Thus, a prolonged aPTT cannot be an obstacle for using anticoagulation therapy in the preventing and treatment of venous thrombosis in these COVID-19 patients.

In our view, it is better that clinicians do not withhold the use of anticoagulants while awaiting more investigations of a prolonged aPTT, especially a disturbed aPTT with high-risk pulmonary embolism alone In

conclusion, due to the importance of recent studies on thrombotic events in the patients with COVID-19 infection which could result in serious complications and mortality in the patients, presence of antiphospholipid antibodies and occurrence of the thrombotic events should be further investigated.

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