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COVID-19 coagulopathy, the evolving story of the clotting disorders associated with COVID-19

COVID-19 has affected over 4 million people worldwide, spreading across the continents.

The substantial mortality in at-risk groups is noted and also the multiple manifestations of the disease.

Among hospital patients with COVID-19, the most frequent complications are pneumonia, sepsis and respiratory failure with some patients developing severe systemic disease and multi-organ failure.

A report from Wuhan in January 2020 suggested elevated D-dimers and prolonged prothrombin times were baseline characteristics of patients critically ill with COVID-19.

It is now found that the burden of these thrombotic complications in these patients has been confirmed. The latest data as detailed in an editorial found in the June edition of The Lancet Haematology suggests that the incidence of thrombotic complications in patients with COVID-19 admitted to intensive care is between 16 to 49%.

It is known that critically ill patients are generally more predisposed to thromboembolism. This can result from the combination of immobility, systemic inflammation, platelet activation, endothelial dysfunction, and stasis of blood flow, which then all lead to coagulation. However, the COVID-19 associated thrombotic complications appear to resemble other systemic coagulopathies found during severe infections such as sepsis-induced coagulopathy or disseminated intravascular coagulations.

Patients with severe COVID-19 not only have elevated D-dimers and fibrinogen but they also have a mild prolongation of prothrombin time and thrombocytopaenia. However, this is uncommon at admission whereas patients with DIC commonly have prolonged prothrombin times and thrombocytopaenia on admission.

As COVID-19 progresses, DIC develops in patients with severe COVID-19. Post-mortem findings show extensive diffuse alveolar damage and thrombi present within small peripheral vessels in the lungs. This microvascular pulmonary thrombosis could cause obstruction of small vessels and organ failure.

When this is compared with the clinical and pathological findings using the data from Wuhan, it is clear that clinical markers of coagulopathy in patients severely ill with COVID-19 are associated with a higher risk of death.

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Currently interim guidance recommends regular monitoring of haemostatic markers such as D-dimers, prothrombin time and platelet count in all patients presenting with COVID-19. The prophylactic use of low molecular weight heparin is also recommended in all hospitalised patients unless there are contraindications.

But the fundamental question which could help prevention, diagnosis and treatment remains unclear. Are the haemostatic changes a consequence of severe inflammation or are they a specific effect mediated by the virus?

In some hospitalised patients with COVID-19, particularly as occurs in sepsis more generally, there exists an overproduction of early response proinflammatory cytokines such as interleukin and TNFa, which then lead to a cytokine storm. This hyperinflammatory state causes lung injury and damage to the microvasculature and endothelial dysfunction which could trigger haemostatic derangement and generation of pulmonary thrombi.

In this situation, it is possible that early intervention which is aimed at reducing inflammation might help prevent thrombosis.

The alternative hypothesis is that the virus directly or indirectly interferes with the coagulation pathways causing systemic thrombosis. In this case, early thromboprophylaxis might be the key to manage the coagulopathy.

For those patients with severe COVID-19, treatment strategies which target inflammation and coagulation might be very promising.

Preliminary evidence suggests that LMWH, which has both anticoagulant and anti-inflammatory effects, might improve prognosis in patients with severe COVID-19 who have the SIC criteria or with elevated D-dimers. At this time other anticoagulants such as antithrombin III, factor Xa, and complement inhibitors, are being trialled.

Many questions, however, remain regarding the efficacy of anticoagulants in severe COVID-19. There are also questions on the timing of the intervention in the course of the disease and the preferred type, dose and duration of treatment all need to be established in prospective studies.

Our haematology colleagues are rising to the challenge and can provide guidance in how to manage COVID-19 associated coagulopathy in the face of much uncertainty.

The London General Practice

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