

How coagulation diagnostics support COVID-19 vaccination and patient management

DOI:- <https://doi.org/10.62772/APFCB-News.2022.1.3>



Contributed by Niti Dawar, MD, Medical & Scientific Affairs Manager (Coagulation), Roche Diagnostics Asia Pacific.



Contributed by Yingli Huang, Product Manager (Core Lab), Roche Diagnostics Asia Pacific.

E-mail: hong-yew.lim@roche.com

Infection with COVID-19 has been associated with thrombosis, or blood clots, involving the veins and arteries. The risk of blood clots is highest for individuals admitted to hospital with COVID-19 infection, occurring in about 5% of people admitted to a regular hospital ward and up to 20% for those in the intensive care unit (ICU), on life-support. The risk of blood clots for individuals with COVID-19 but not requiring admission to hospital is lower at about 1% [1].

While highly uncommon, vaccination with adenovirus-based vaccines is also associated with blood clots through a condition called vaccine-induced thrombotic thrombocytopenia (VITT). To better understand the key coagulation risks and considerations around COVID-19 vaccination and patient management, Roche Diagnostics Asia Pacific recently spoke with Dr. Ng Heng Joo, Senior Consultant & Head of Department of Haematology at Singapore General Hospital.

Coagulation markers in COVID-19 care and post-vaccination evaluation
Accumulating laboratory evidence indicates that abnormal coagulation changes in COVID-19 infected patients may be a result of profound inflammatory response, and not associated with intrinsic procoagulant effect itself. Marked increases in coagulation proteins may occur in patients with severe COVID-19 infection, consistent with a profound acute-phase response. A subset of severe pneumonia patients developed viral sepsis, disseminated intravascular coagulation (DIC), and multi-organ failure.

Since D-Dimer is a positive marker for patients with thrombosis, studies have been done that attempt to incorporate D-Dimers into predicting the severity for COVID-19. "D-Dimer has been incorporated into some of these risk assessment scores for development of venous thromboembolism in COVID-19 patients," notes Dr. Ng. "It has been a bit difficult to define cutoff levels that constitute concern about increasing severity of the disease and how that would impact the escalation of therapy for patients."

"Common examples of some of the risk assessment models that were used include the Improved D-Dimer score as well as the Caprini score," he adds. "There have been some validation studies that show it works pretty well in helping to predict which of the patients can be classified as either low-risk, intermediate-risk or high-risk of developing venous thromboembolism and arising from that, the appropriate use of anticoagulation therapy for patients."

For patients with VITT, testing typically reveals low fibrinogen and very raised D-Dimer levels above the level typically expected in venous thromboembolism. "We know the potential onset for VITT usually is between 5 to 28 days post vaccination," highlights Dr Ng. "We do know that it causes unusual sites of thrombosis like cerebral venous sinus thrombosis splenic vein thrombosis."

Antibodies to platelet factor 4 (PF4) have been identified in patients with VITTence there are similarities to heparin-induced thrombocytopenia (HIT) despite the absence of prior exposure to heparin treatment. The anti PF4 antibodies can be detected by the ELISA HIT assay but not usually with the rapid tests which are usually based on chemiluminescence as well as latex assays.

Challenges in a coagulation laboratory in the COVID-19 era

By way of its association with thrombosis, COVID-19 has certainly brought on many challenges for patient diagnosis and management. In the early phase of the pandemic, one of these challenges was understanding the pathophysiology or the role of thrombosis in patients with COVID-19. Therefore, trying to stratify who is at high risk and the role of anticoagulation therapy for that group of patients has been challenging.

Another diagnostic challenge has been the entity of VITT. While the test against anti-PF4 antibodies has been well established for HIT, its use and its sensitivity for patients with VITT have been distinct and different. As a further adjunct to just the demonstration for anti-PF4 antibodies, there have been additional tests that have been developed to confirm the presence of antibodies that activate platelets [2].

This challenge led to the development of additional tests utilising what's available for example, the heparin-induced platelet aggregation assay (HIPAA). As a modification of the HIPAA test, investigators developed a platelet factor 4 induced platelet aggregation test to try to better define the aetiology or rather the diagnosis of patients with VITT. Platelet activation or the antibodies by using flow cytometry have been used as tests in the laboratory. These tests are useful as well as challenging to develop but they are diagnostic of VITT.



A new generation for coagulation diagnostics

COVID-19-induced coagulopathy is a distinct entity that exhibits a marked elevation of D-Dimer. COVID-19 is associated with high risk of micro- and macrovascular thrombosis and raised incidence of anticoagulation failure. Unlike conventional sepsis, anticoagulation plays a key role in the management of COVID-19 with a positive impact on survival. The biomarkers and the various scoring systems may be helpful in triaging patients to risk categories for the purpose of anticoagulation as well as diagnosing post-vaccination clots in COVID-19.

References

1. ISTH experts explain new Blood Clotting phenomenon in hospitalized COVID-19 patients. <https://www.isth.org/news/516793/ISTH-Experts-Explain-New-Blood-Clotting-Phenomenon-in-Hospitalized-COVID-19-Patients-.html>.
2. Pathologic Antibodies to Platelet Factor 4 after ChAdOx1 nCoV-19 Vaccination <https://www.nejm.org/doi/full/10.1056/NEJMoa2105385>.
3. COVID-19 vaccines, blood clots and anticoagulation therapy: insights from Dr Ng Heng Joo <https://www.labinsights.com/get-inspired/content/covid-19-vaccines-blood-clots-and-anticoagulation-therapy-insights-dr-ng-heng-joo>.

