Letter to the Editor

COVID-19 and thrombosis

Sir,

The first case of novel corona virus disease (COVID-19) was reported in China and undoubtedly today this disease has rapidly crossed borders, infecting people throughout the world. There are heaps of complications related to COVID-19 namely acute respiratory failure, acute liver and kidney injury, bacterial and fungal infections, and septic shock. Vascular thrombosis is another burden that COVID-19 is piling on to the load of its complications. Venous thromboembolism namely deep vein thrombosis and pulmonary thromboembolism; pulmonary microvasculature thrombosis and systemic arterial thromboembolic events like limb ischemia, myocardial ischemia/infarction and cerebrovascular thrombosis are being increasingly reported in COVID-19 patients.^{1,2}

SIGNS AND SYMPTOMS

The whole complex of symptoms of COVID-19 seems to be due to vascular thrombosis/inflammation. Cerebrovascular – ischemic infarcts causing limb weakness/paralysis; myocardial infarction – coronary artery thrombosis causing chest pain and cardiac arrest; pulmonary major and micro vascular thrombosis causing dyspnea, cough and hypoxia; arterial thrombosis causing limb ischemia with cramping pain, discolouration and gangrene; deep vein thrombosis causing mild to severe swelling in the limbs and also sometimes leading to intra-cardiac clots leading to life threatening hypoxia; elevated blood sugar levels possibly due to micro-thrombi in the pancreatic vasculature; renal dysfunction possibly due to intra renal micro-vascular thrombosis; and finger and toes showing discolouration possibly due to micro-vascular thrombosis/vasculitis.

THEORETICAL BASIS FOR CAUSATION

Clotting occurs when the novel coronavirus attacks the endothelial cells that line the blood vessels. The virus does this by binding to the angiotensin converting enzyme-2 (ACE-2) receptors, which are present in the endothelial cell membrane. As soon as the virus binds to these receptors, the blood vessels start releasing proteins that trigger blood clotting.³

Another theory explains it as COVID-19 causes the body's immune system to trigger a hyperactive inflammatory response, which leads to inflammation and may then trigger clotting. Exaggerated inflammatory response leads to but not limited to: inflammatory cytokines (e.g. IL-6) mediated activation of vascular endothelial cells and

increase in fibrinogen levels; and endothelial injury leading to elevated plasminogen activator inhibitor-1 (PAI-1) levels; fibrinolysis is impaired due to elevated PAI-1 levels; and endotheliopathy causing elevated Von Willebrand factor (VWF), and platelet activation causing hypercoagulopathy.⁴

DIAGNOSTIC INVESTIGATIONS

Thrombosis or thrombotic potential should be evaluated using - Blood Investigations like C-reactive protein and inflammatory markers like IL-6, fibrinogen level, activated partial thromboplastin time (aPTT), prothrombin time (PT)/international normalized ratio (INR), D-dimer, platelet count, soluble thrombomodulin, VWF level/antigen; and radiological investigations like duplex/Doppler ultrasound, computed tomography (CT)/magnetic resonance imaging (MRI) of brain with angiography and pulmonary/peripheral angiography.

CURRENT MANAGEMENT AND RECOMMENDATIONS

Patients' hydration status should be well maintained. Current management is mainly focused on the routine weight based anticoagulation like heparin or low molecular weight heparins. Is the standard weight-based prophylactic anticoagulation sufficient or not, needs to be evaluated. An anticoagulation protocol needs to be created that is not only based on the weight of the patient but also takes into consideration various other patients factors like the blood levels of the procoagulant inflammatory markers. Role of antiplatelet and platelet activity stabilizing medications need to be evaluated.

Wider use of fibrinolytic agents should be studied to know their advantages and understand their right dosing. Vascular endothelial stabilizing medications need to be considered. Interactions of oral anticoagulants and antiplatelet medications with antiviral or other newer COVID-19 therapeutics should also be considered.⁵

CONCLUSION

It is apparent that thrombosis has a key role in the pathogenesis, clinical effects and complications of COVID-19.

Further research to early control this significant thrombotic effect of COVID-19 infection will definitely help in curtailing the morbidity and mortality associated with this disease.

**Kavita Verma¹, Anjali Sharma^{2*},
Shahzad Sarosh Bulsara³**

¹Child Health Nursing, ²Community Health Nursing,
Eternal University, Akal College of Nursing, Baru Sahib,
Himachal Pradesh, India

³Peripheral Vascular Surgeon and Endovascular
Specialist, Kaushalya Hospital Nashik, Maharashtra

***Correspondence to**

Anjali Sharma

E-mail: anjali11340@gmail.com

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