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Neurological manifestation and Coagulation abnormalities and Thrombosis in patients with COVID-19- An observational study and review of literature

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ABSTRACT

COVID-19 Virus disease pandemic is a challenge faced by mankind in the age of globalization. The novel coronavirus SARS-CoV-2 can survive in the air for several hours in fine particles known as aerosols, according to preliminary research. Coronavirus disease 2019 (COVID-19) predominantly have a respiratory tract infection, a proportion of patients progress to a more severe and systemic disease, characterised by acute lung injury with acute respiratory distress syndrome (ARDS), shock, and multiple organ dysfunction (like brain, kidney), associated with substantial mortality. This is an observational study of 174 patients admitted in covid Isolation ward at SVBP Hospital, Meerut. CNS manifestations of corona disease were observed in covid -19 positive patients. Headache, anxiety , depression, and ischaemia of brain parenchyma leading to infarct were common sign and symptoms.

Keywords: Covid -19, CNS manifestation, Thrombosis, Coagulation abnormalities

INTRODUCTION

Although most patients with coronavirus disease 2019 (COVID-19) predominantly have a respiratory tract infection, a proportion of patients progress to a more severe and systemic disease, characterised by acute lung injury with acute respiratory distress syndrome (ARDS), shock, and multiple organ dysfunction (like brain, kidney), associated with substantial mortality. Many patients with severe COVID-19 present with coagulation abnormalities that mimic other systemic coagulopathies associated with severe infections, such as disseminated intravascular coagulation (DIC), but COVID-19 has distinct features. Coagulopathy in patients with COVID-19 is associated with an increased risk of death. The most typical finding in patients with COVID-19 and coagulopathy is an increased Ddimer concentration, a relatively modest decrease in platelet count, and a prolongation of the prothrombin time. Thrombocytopenia and prothrombin time in

COVID-19 have not been found to be an important predictors of disease progression or adverse outcome. The combination of thrombocytopenia, prolonged prothrombin time, and increased D-dimer is suggestive of DIC, although the pattern is distinctively different to DIC seen in sepsis. In sepsis, thrombocytopenia is usually more profound, and Ddimer concentrations do not reach the high values seen in patients with COVID-19. Post- mortem findings in patients with COVID-19 show typical microvascular platelet-rich thrombotic depositions in small vessels of the lungs and other organs. Taken together, available evidence suggests that the coagulopathy associated with COVID-19 is a of low-grade DIC & localised combination pulmonary thrombotic microangiopathy, which could have a substantial impact on organ dysfunction in the most severely affected patients. We report the neurological features in an observational series of 174

patients of COVID19 admitted in SVBP Hospital, Meerut (U.P.), INDIA till 30 April 20.

Pathogenesis

Severe COVID-19 is associated with increased concentrations of proinflammatory cytokines, such as tumour necrosis factor- α (TNF- α) and interleukins (IL), including IL-1 and IL-6. IL-6 can induce tissue factor expression on mononuclear cells, which subsequently initiates coagulation activation and thrombin generation. TNF- α and IL-1 are the main mediators driving a suppression of endogenous anticoagulant pathways.

Coronavirus infections are also associated with a remarkable activation of the fibrinolytic system. Inflammation-induced endothelial cell injury could result in massive release of plasminogen activators, which could explain the high concentrations of D-dimer and fibrin degradation products in patients with severe COVID-19. Thrombotic microangiopathy is typically caused by pathologically enhanced platelet-vessel wall interaction.

Observation at SVBP Hospital, MEERUT

Neurological Manifestations	No. of patients	Percentage of patients	Remark
Headache	102	58.62%	
Irritability	58	33.33%	
Combined Anxiety and depression (CAD)	124	70%	
Ischaemic stroke	8	4.5%	Numbness & weakness of lower and upper limbs, dysarthria
Diffuse corticospinal tract sign	72	41.37%	
Space occupying lesion	01	Coincidental finding	Death
Death	12	6.8%	

Table No.1

Total of 174 patients admitted to our hospital till date, total of 8 patients presented with features of stroke(numbness & weakness of lower and upper limbs, dysarthria,) CT evaluation of these patients wereshowing hypodensities suggestive acute infarct (one of them aged 44 years, came with CT films

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which shows infarct of right MCA region with paralysis of left side of face, arm and leg on evaluation he was suffering from headache, cough & chills from past few days and develop these features within 2 days and had no comorbidities.) Many patients with severe form of disease (RR >26/min,sp02 < 92% on air) after admission had slight increase in prothrombin time and modest decrease in platelet counts further investigations(like D- dimer, fibrinogen, serum ferritin) were not available, these results were enough at least to consider covid-19 as a prothrombotic disease.

Discussion

A retrospective study done in China that included 449 patients admitted to hospital with severe COVID-19 infection showed a lower mortality in patients with COVID-19-associated coagulopathy who received prophylactic heparin than in patients not receiving anticoagulant treatment. As suggested by the studies in which corona patients presenting with stroke features published in NEJM, D-Dimer was consistently increased in these patients and anticoagulation therapy were instituted earlier in these patients which shows positive results. Autopsy results in Italy also shows thrombosis in patients infected with coronavirus. From various studies till date it has been concluded that D-dimer can be used as a prognostic factor for predicting mortality in serious covid-19 patients, therefore, anticoagulants can be instituted on the basis of its values:

Table No	0.2
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D-Dimer	Anticoagulation drugs dosing		
<1 mg/L	Prophylactic dose given (Enoxaparin 40mg, subcutaneously, QID).		
1-2 mg/L	Prophylactic dose should be given, if, D-dimer showing increasing trend, then regime should be shifted to therapeutic anticoagulation.		
>2mg/L	Therapeutic anticoagulation (Enoxaparin 1 mg/kg, subcutaneously, 12hourly.		

These are the broad guidelines taken from Massachusetts general hospital article on haematology recommendations and dosing guidelines during COVID -19(factors like creatinine clearance, obesity (BMI > 40), hepatic clearance were not taken into account, these factors should be individualized according to the patient.

Conclusion

Using the available evidence, we suggest monitoring coagulopathy in patients with severe COVID-19 by measuring prothrombin time, platelet count, and D-dimer concentrations every 2–3 days. There is evidence supporting the use of prophylactic dose low molecular weight heparin (LMWH) as prophylaxis for venous thromboembolism in critically ill patients. In view of the hypercoagulable state of patients with severe COVID-19, and the potential increased risk of

thrombosis, we suggest that all patients with COVID-19 that are admitted to hospital should receive this prophylactic treatment in the absence of medical contraindications and the patients with severe disease should receive therapeutic anticoagulation. All patients showing symptom of neurological must be investigate with involvement CT SCAN/MRI scan brain for stroke and anticoagulant therapy should be given.

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