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COVID-19 AND COAGULATION ABNORMALITY

General Medicine

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ABSTRACT

The pandemic of coronavirus disease 2019 (COVID-19) infection has emerged as a serious health crisis. Although the majority of the patients predominantly have a respiratory tract infection, while 5-15% of the patient progress to severe disease and critical illness with multisystem involvement. Coagulation system involvement with different coagulation abnormalities is seen in severe and critical patients with increased mortality. The common coagulation abnormalities frequently seen in COVID19 infection are DIC, thromboembolism, thrombocytopenia and increased D-dimer. The coagulation abnormalities in COVID-19 are slightly different from those seen in sepsis. The increase level of D-dimer is common with profoundly increase in severe disease resulting in a poor prognostic factor. Severely affected patients should be routinely screened with D-dimer, platelet count and PT daily or on alternate day. The suspected case of VTE and PE should go for an early investigation. The prophylaxis with LMWH should start in all severely ill and ICU admitted patients in absence of contraindication.

KEYWORDS

Covid-19, Coagulation and D-dimer

INTRODUCTION:

The pandemic of coronavirus disease 2019 (COVID-19) infection has emerged as a serious health crisis with grave consequences worldwide (more than 635,000 deaths till now).[1] The viral infection has become more problematic as no specific proven antiviral treatment is available as of now. The patient's presentation varies from being asymptomatic to severely critically ill with multiple organ failures, which become the causative factor for the mortality.[2,3] Although the majority of the patients predominantly have a respiratory tractinfection. While 5-15% of the patient progress to more severe disease and critical illness, like treatment-resistant fever, respiratory failure, acute lung injury, acute respiratory distress syndrome (ARDS), septic shock, and multiple organ dysfunction.[3,4] Besides the above finding, various studies from all over the world have shown that the coagulation abnormality is seen in severe form of COVID-19 infection.[5-11] The various coagulation abnormalities in COVID-19 infection are thromboembolism, disseminated intravascular coagulation (DIC), thrombosis, thrombocytopenia, increase D-dimer and diffuse alveolar damage.[7-12] The abnormal coagulation is associated with poor prognosis and higher mortality.[7,9,10] The relevance of coagulation abnormalities in COVID-19 infection are becoming increasingly clear as the patients with severe diseases, sometimes develop asymptomatic or symptomatic coagulation abnormality with or without their complications.[7,9-11,13] In this review we have discussed the various coagulation abnormalities of COVID-19, current problems and potential prevention and treatment interventions.

D-dimer:

One of the main findings in COVID-19 patient's coagulopathy is an increased D-dimer level. It is a degradation product of fibrin and reflects blood clot formation and its subsequent fibrinolysis. The sensitivity of D-dimer for thrombotic disease is very high, but has poor specificity. The different studies of COVID-19 patients have consistently found a very strong association between high level of D-dimer and severity of disease with poor outcome. Guan W et al in a study of 1099 COVID-19 patients from China, found raised D-dimer of >0.5mg/dl in 260(46%) of their 560 patients. They found that the level of D-dimer was higher (59%) in severe disease compared to non-severe diseases (43%).[14] Tang N et al in an observational study of 183COVID-19 patients in China found that the mean D-dimer level was 0.66μg/ml (range 0.38-1.50). The level was significantly higher in patients who didn't survive 2.12μg/ml (range 0.77–5.27) compared to survivors with 0.61μg/ml(0.35–1.29).[7] In a study of hospital admitted COVID-19 pneumonia patients the median D-dimer level was higher (2.4μg/ml,IQR 0.6–14.4) in patients admitted to the intensive care unit (ICU) than those who did not required ICU care (0.5μg/ml, 0.3–0.8).[6] In another retrospective study of 191 patients from China, it was found that the on admission median D-dimer was 0.8μg/ml (0.4 -3.2). It was significantly higher in non-survival patients (5.2, 1.5–21.1) compared to survivors (0.6, 0.3–1.0). The D-dimer level was >1μg/ml in 81% of the non-survivor and 24% of the survivors. They found the increasing odd of in hospital death 18-times with D-dimer >1μg/ml (95% CI 2.6–128.6; p=0.0033).[15] Chen G et al in a study of moderate to severely infected COVID-19 patients, found that the median D dimer level was 0.5μg/ml (0.4–1.8). The level was markedly higher in severe cases (2.6, 0.6–18.7) than in moderate cases (0.3, 0.3–0.4).[16] In a retrospective, single-centre case series of the 138coronavirus infected pneumonia patients from Wuhan found that the median D-dimer level was 2.03μg/ml (1.21-4.03). The level was significantly higher in ICU patients (4.14, 1.91-13.24) compared to non-ICU patients (1.66, 1.01-2.85). The level was also significantly higher in non-survivors compared to survived patients.[17] Panigada M et al in a study of 24 intubated Covid-19 patients found high level of D-dimer with a mean of 4.87μg/ml (1.19-16.95).[18] Li X et al in a study of 25 death cases of COVID-19 patient found that the level of D-dimer was increasing in 75% cases from first test with 1.18μg/ml (0.42–4.04) to last test before death 9.93μg/ml (2.65–54.8). They concluded that the rising of D-dimer levels can be used as indicators of the disease progression.[19] Chen T et al in a retrospective study of 799 (113 deceased) patients from Tongji hospital China found that the median D-dimer was raise with 1.1 μg/mL (0.5-3.2). It was significantly higher in patients who died 4.6ug/ml (1.3-21.0) compared to recovered patients 0.6ug/ml (0.3-1.3).[20] Wu C et al in a study of 201 COVID-19 patients found that the median level of D-dimer was significantly higher in ARDS patients with 1.16ug/ml(0.46-5.37) compared to non ARDS patients 0.5ug/ml(0.33-0.93). Even amongst the ARDS patients the level was significantly higher in deceased patients with 3.95ug/ml (1.15-10.96) compared to alive ARDS patients 0.49ug/ml (0.31-1.18).[21] The various studies of D-dimer level regarding severity/ICU care and non-survival patients are summarized in table1.

The level of D-dimer increased in COVID-19 infection. The level is higher in severe form of the disease, who required ICU treatment. The level was significantly higher in non-survival patient compare to survivors. It is also increases with progression of the diseases with its duration. So D-dimer can be used for diagnosis of disease with other clinical and laboratory parameters. It can also be used as prognostic marker to monitor disease progression, ICU care admission/

management and response to treatment. It should be repeated every 2-3days for management of coagulopathy in severe COVID-19 infection.

Tables and legends

Table 1: Summary of D-dimer level with severity/ICU care and non-survival patients

Author (reference)	N	D-dimer (µg/ml)	Severe / ICU	Non-severe/ Non ICU	Survivor	Non-survivor
Guan W et al (14)	1099	>0.5mg/dl in 46% cases	59% cases	43% cases	____	_____
Chen T et al (20)	799	Median 1.1(0.5-3.2)	_____	_____	0.6 (0.3-1.3)	4.6(1.3-21.0)
Wu C et al (21)	201	_____	0.5(0.33-0.93)	1.16(0.46-5.37	0.49(0.31-1.18)	3.95(1.15-10.96)
Zhou F et al (15)	191	Median 0.8 (0.4 -3.2)	_____	_____	0.6, 0.3–1.0	5.2, 1.5–21.1
Tang N et al (7)	183	Mean 0.66 (0.38-1.50)	____	____	0.6(0.35–0.29)	2.12(0.77–5.27)
Wang D et al (17)	138	Median 2.03 (1.21-4.03	4.1(1.9-13.24)	1.6(1.0-2.85)	_____	Higher than survivor
Huang C et al (6)	41	Median 0.5 (0.3–1.3)	2.4(0.6–14.4)	0.5 (0.3–0.8)	____	____
Chen G et al (16)	21	Median 0.5 (0.4–1.8)	2.6(0.6–18.7)	0.3(0.3–0.4)	_____	_____
Panigada M et al (18)	24	Mean 4.87 (1.19-16.95	_____	_____	_____	_____
Li X et al (19)	25	Increases in 75% cases	_____	_____	_____	_____

Thrombocytopenia:

Thrombocytopenia is independently associated with the severity of the disease and risk of mortality in ICU admitted patients.[10,22] Various studies have reported low platelet count in COVID-19 infection.[6,10,14] Guan W et al. in a study of 1099 COVID-19 patients from China, found the low platelet count of <1.5lakh/µl in 315(36%) in their 869 cases. The thrombocytopenia was more in severe disease (58%) compared to non-severe disease patients (32%).[14] Huang C et al in a study of an hospital admitted COVID-19 pneumonia patients found that thethrombocytopenia with platelet count <1.0lakh/µl was seen in 5% of their 41 cases.[6]Wang D et al in a retrospective, study of the 138 COVID-19 pneumonia patients from Wuhan found that the median platelet count was 1.63lakh/µl (1.23-1.91). However the platelet count was lower in ICU admitted patients with 1.42lakh/µl (1.19-2.02) compared to non- ICU patients 1.65lakh/µl(1.25-1.88).[17] Zhou F et al. in a retrospective study of 191 patients from Wuhan found that the median platelet count was normal with 2.06lakh/µl (1.55–2.62). However, it was significantly lower in non-survival patients (1.65, 1.07–2.29) compared to survivors (2.22, 1.68–2.71) with p value <0.0001.[15]Lui Y et al in a study of 12 COVID-19 pneumonia and ARDS patients found that the decreased platelet count (<1.5lakh/µl) in 42% of the patients with range from 0.9-1.2lakh/µl.[23] Liu W et al in a study of 78 patients with COVID-19-induced pneumonia found that the mean platelet count was 1.69±0.57 lakh/µl. The platelet count was decreased to 1.43±0.64lakh/µl in clinically progressed group patients, while it was increases to 1.73±0.55 in a clinically improved group. They found that the platelet count was not a risk factors for the disease progression on logistic analysis with odd ratio (OD, 2.259, 95%CI, 0.394–12.958, P= 0.360).[24] Tang N et al. in a study of 449 severe COVID patients found that the platelet count was normal with 2.1±1.0lakh/µl. However the level was significantly lower in non-survivals (1.78±0.92) compared to survivors (2.31±0.99) with p<0.001.They concluded that the platelet count was negatively correlated with 28-day mortality in multivariate analysis.[25]Chen T et al. in a retrospective study of 799 with 113 deceased patients from China found that the median platelet count was 1.79lakh/ul (1.33-2.35). However the count was significantly lower in deceased patient 1.56lakh/ul (1.11-2.19) compared to recovered patients 1.98 (1.60-2.56).[20]The various studies on platelet concerning severity/ICU care required and non-survival patients are summarized in table2.

Table 2: Summary of platelet count with severity/ICU care and non-survival patients

Author (reference)	N	Platelet count (Lakh/µl)	Severe / ICU	Non-severe/ Non ICU	Survivor	Non-survivor
Guan W et al (14)	1099	<1.5 in 36% cases	58% cases	32% cases	____	_____
Chen T et al (20)	799	Median1 .7(1.33-2.35)	_____	_____	1.98 (1.60-2.56)	1.56(1.11-2.19)
Tang N et al (24)	449	Mean 2.1±1.0l	_____	_____	2.31±0.99	1.78±0.92
Zhou F et al (15)	191	Median 2.0(1.55–2.62)	_____	_____	2.22 (1.68–2.71)	1.65 (1.07–2.29)
Wang D et al (17)	138	Median1.6(1.23-1.91)	1.42l(1.19-2.02)	1.65(1.25-1.88)	_____	_____
Liu W et al (23)	78	Mean 1.69±0.57	1.73±0.55	1.43±0.641		
Huang C et al (6)	41	Median 1.64 (1.3–2.63) with <1.0 in 5% cases	1.96 (1.6–2.63)	1.49 (1.31–2.63)	____	____
Lui Y et al(22)	12	<1.5 in 42% (0.9-1.2l)	_____	_____	_____	_____

Lippi G at al in a meta-analysis of 9 studies of thrombocytopenia including 1779 COVID-19 patients concluded that the platelet was significantly lower in more severe diseases. In a subgroup analysis compared by survival, it was found an even lower platelet count was observed with mortality and the low count is associated with over 5fold increased risk of severe diseases.[10]The platelet count did not decreased uniformly in all COVID-19 patients. The platelet count was decreased in the range of 5-42% patients in different studies. The lowered count was more commonly associated with the severe form of the disease than mild to moderate form of disease. Even in normal level platelet count studies shown that the level is lower in non-survival and ICU admitted patients. Few studies have found that the platelet count is negatively correlated with mortality. There by it can be used as a prognostic marker to monitor disease progression, ICU care admission/management and response to treatment. It should be repeated every day in ICU or severe disease for management of coagulopathy.

Disseminated intravascular coagulation (DIC):

DIC is a syndrome characterized by the systemic activation of blood coagulation, which generates intravascular thrombin and fibrin, resulting in the thrombosis of small to medium sized vessels and ultimately organ dysfunction and severe bleeding.[26] The various common markers for DIC are thrombocytopenia, prolonged prothrombin time (PT), prolonged activated partial thromboplastin time (APTT), increased D-dimer, increased fibrinogen degradation products (FDP), decreased fibrinogen and increased von Willebrand Factor, hence no single marker alone can be used to diagnose DIC alone.[27,28] Various published reports have found that COVID-19 infection associated with DIC.[4,7,12,28,29] The combination of prolonged PT, decreased platelet count and increased D-dimer is suggestive of DIC, although the pattern is different from sepsis DIC.[30] However the DIC in COVID-19 infection is slightly different from having higher D-dimer and less profound thrombocytopenia. So as per the International society on thrombosis and haemostasis most of the DIC in COVID-19 infected patients did not fit the DIC diagnosis criteria.[4,7,30]Tang N et al. in one Chinese single-centre retrospective cohort study from Tongji hospital of Huazhong university of science enrolled 183 patients with COVID-19 infection for evaluation of DIC. They found that as per international society on thrombosis and haemostasis diagnostic criteria for DIC,[26] 15(71.4%) of non-survivor and one (0.6%) of survivor was classified as having overt-DIC (≥5 points) in later stages of novel coronavirus pneumonia, the median time from admission to DIC was 4 days (range, 1-12 days).[7]Guan W et al. in a study of 1099 COVID-19 patients from China, found the only one case (0.6%) of DIC in 173 severe cases, while there was no any DIC among 926 non-severe diseases.[14]Chen T et al. in another retrospective study with 113 deceased patients from Tongji hospital, Wuhan China found that the DIC was seen in 21(8%) of the total 274 corona virus infected cases. DIC was significantly higher in dead patient 19(17%) compared to 2(1%) in recovered one.[20]Tang N et al. in a study of 449 severe COVID patients found that the sepsis-associated DIC was 97 (21.6%) as per new category of international society of thrombosis and haemostasis SIC criteria (total score ≥ 4). They found that the DIC was significantly higher in non-survivor with 55 (41.0%) compared to survivor 42 (13.3%) with p value <0.001.[25]Deng Y et al in a study of 964 patients from Wuhan, China found that the DIC was significantly higher in 109 deceased patient with seven (6.4%) compared to no DIC in 116 recovered patients with p value of 0.006.[31]The various studies of DIC about the severity and non-survival/deceased patients are summarized in table3.

Over all there is no specific study of DIC among COVID-19 patients. The studies on DIC were primarily with other primary end points. With a limited available data, the DIC was seen in <1% to 71% cases of severe COVID-19 infection. The DIC is more common in severe form of the disease and associated with high mortality. The DIC of COVID-19 has also not fulfilled all the criteria of sepsis DIC. So any suspected case should be investigated for DIC and early treatment should be started to prevent complication and decrease mortality.

Table 3: Summary of DIC with severity and non-survival patients

Author (reference)	N	DIC	Severe	Non-severe	Survivor	Non-survivor
Guan W et al (14)	1099	One case	1(0.6%)	Nil	____	_____
Deng Y et al (31)	964	7(3.1%)	_____	_____	Nil	7(6.4%)
Chen T et al (20)	799	21(8%)	_____	_____	2(1%)	19(17%)
Tang N et al (24)	449	97 (21.6%)	_____	_____	42 (13.3%)	55 (41.0%)
Tang N et al (7)	183	16(8.7%)	_____	_____	1(0.6%)	15(71%)

Thromboembolism:

The abnormal coagulation associated with COVID-19 infection suggests the presence of a hypercoagulable state that might increase the risk of thromboembolic complications. Other factors that can increase the risk of thrombosis are excessive inflammation, hypoxia, vascular injury, immobilisation and DIC.[14,15,17]Panigada M et al from Italy found that the hypercoagulability state on thromboelastography among their intubated COVID-19 patients. They concluded that the hypercoagulability is due to the a profound derangement of hemostasis and is the likely contributor to pulmonary embolism and/or deep vein thrombosis of the lower limbs observed in patients with Covid-19.[18] According to the published studies the incidence of thromboembolic complications in COVID-19 patients is varying from 15–45%.[4,11,12,32] Klok FA et al studied 184 ICU patients with COVID-19 pneumonia for occurrence of venous and arterial thrombotic events, including deep vein thrombosis(DVT), pulmonary embolism (PE), ischemic stroke,myocardial infarction and systemic arterial events. They found that the composite incidence of thrombotic events was 31%. Venous thromboembolic events on CTPA and/or ultrasonography were the most common (27%) and PE was the most frequent thrombotic complication in 25/31(81%) patients.[11] Helms J et al. from two French tertiary hospitals study, reported the occurrence of thrombotic events in 150 Covid-19 ARDS patients admitted in ICU. They found that the 64 clinically relevant thrombotic complications were diagnosed during their ICU stay. PE was the most common complication seen in 25(16.6%) patients. It was further reported that 28/29 (96.6%) patients receiving continuous renal replacement therapy experienced circuit clotting and 3 thrombotic circuit occlusions in 12 patients requiring extracorporeal membrane oxygenation for refractory hypoxemia.[32]Cui S et al from Wuhan, China found that the incidence of venous thromboembolism (VTE) in severe novel corona virus pneumonia patients was 20/80(25%), with mortality in 8(40%) patients. The VTE group were significantly older age, had lower lymphocyte counts, longer APTT and hihger D-dimer compared to non VTE patients. They also concluded that the D-dimer have of sensitivity 85.0%, specificity 88.5%, and negative predictive value (NPV) 94.7% for predicting VTE if the cut off level is 1.5 µg/mL.[9] Lorant IL et al in a study from France including 106 COVID-19 patients found that 32/106(30%) patients with pulmonary CT angiogram were tested positive for acute pulmonary embolus. These patients with PE had higher D-dimer level, likely to be in the ICU and more often treated with LMWH before CT angiography compared to the patients without PE. They also found that D-dimer of 2.6µg/mL had sensitivity of 100% and specificity of 67% for PE on CT angiography.[33] Thromboembolism is a common complication with high mortality in sepsis, ICU patients and ARDS patients. There is a lack of data on prevalence of thromboembolism specifically in COVID-19 infection as its etio-pathogenesis is not fully clear and is in an evolving state till date. The available published reports have found the incidence of 15-45%. Clinically suspected cases of COVID infection should be screen for all thromboenbolic complications to prevent and early start treatment for its better management and reduce mortality.

Others:

The other coagulation abnormalities seen in COVID-19 infection are increased PT, APPT, lactate dehydrogenase (LDH),fibrin degradation products (FDP), fibrinogen levels. antithrombin activity (AT) level and high ferritin concentrations.[4,15,34]Wu C et al in a study of 201 COVID-19 pneumonia patients found that the increased PT was associated with increased risk of ARDS ($p<0.001$).[21] In another retrospective study by Tang et al, of 183 consecutive COVID-19 patients, it was found that the non-survivors had significantly higher FDP levels, prolonged PT and APTT compared to survivors at the initial evaluation. By the late hospitalization, the AT levels were also lowered in non-survivors.[7]Han H et al in a prospective study evaluating the coagulation profile of patients with COVID-19 infection found that the FDP and fibrinogen levels were markedly higher among patients compared with the healthy controls ($p<0.001$). The patients with severe the disease showed higher value FDP than those with milder manifestations ($p<0.05$).[35] Shi S et al in a study of 416 COVID-19 infection patients concluded that the patients presenting with cardiac injury are more prone to coagulation disorders compared with those without cardiac involvement ($p=0.02$).[36] Gou T et al in a study of 187 COVID-19 infected patients found that the patients with high troponin-T levels were presented more frequently with elevated PT, APTT and D-dimer significantly compared to normal troponin-T levels patients.[37] The postmortem findings of COVID-19 infected patients showed typical microvascular platelet-rich thrombotic depositions in small vessels of the lungs and other organs. Diffuse alveolar damage is also a common autopsy finding in COVID-19 infected patients. The various pathological findings were pulmonary microvascular thrombosis and necrosis in mediastinal lymph nodes and the spleen.[4,12,38]

Guidelines and Consensus Statements for Abnormal Coagulation

Various guidelines published some recommendations for the diagnosis and treatment of abnormal coagulation in COVID-19 infection. The few guidelines and their statement summary are:

1. The International Society on Thrombosis and Haemostasis published an interim guidance statement for the recognition and management of coagulopathy in Covid-19. The document highlights several key factors, including an elevated D-dimer and its association with poor clinical outcomes, lack of thrombocytopenia, and late onset DIC in some patients. They recommended monitoring the patient with D-dimer, prothrombin time, platelet count and fibrinogen level for admission, discharge and treatment. Also advised to keep platelet above 0.25lakh/µl in non bleeding patients and platelet above 0.50lakh/µl, fibrinogen above 1.5g/L and PT ratio <1.5 in bleeding patients. The recommendation for treatment with LMWH at prophylaxis doses should be considered in all patients who require hospitalization and absence of any contraindications.[13]
2. The American College of Cardiology recommended pharmacological VTE prophylaxis in Covid-19 patients requiring ICU care as well as those with pneumonia, respiratory failure or other comorbid factors such as heart failure, cancer, prolonged periods of immobility, and possibly pregnant women who are hospitalized and no contraindication.If pharmacological prophylaxis is contraindicated, it is reasonable to consider intermittent pneumatic compression. If VTE prophylaxis is considered, enoxaparin 40mg daily or similar LMWH regimen (e.g. dalteparin 5000U daily) can be administered. Extended post discharge prophylaxis was considered reasonable for high risk patients (reduced mobility, co-morbid factors such as active cancer and possibly an elevated D-dimer at the time of discharge).[39]
3. A consensus statement from several national Chinese societies and working groups highlighted the importance of thromboprophylaxis and vigilant monitoring for thrombotic complications among patients with Covid-19 infection.The consensus statement for prevention and treatment of venous thromboembolism associated with coronavirus disease 2019 infection from China recommended: a) For all severe and critically ill patients having high risk of VTE, prevention is strongly recommended in absence of contraindication. It is also recommended to use intermittent pneumatic compression in high risk of bleeding or with active bleeding contraindicating pharmacological thromboprophylaxis. Patient with signs of massive or high-risk PE in combination with echocardiogram finding, rescue thrombolytic therapy is recommended. For refractory circulatory collapse or cardiac arrest patients, ECMO may be considered, in combination with surgical embolectomy or

catheter-directed treatment. b) Mild and moderate patients presenting acute medical diseases and assessed to have a high or moderate risk of VTE, pharmacological prevention should be prescribed and LMWH is recommended as first line treatment, in the absence of contraindication. c) In case of DVT or PE suspicion, diagnosis should be primarily based on careful bedside clinical examinations and then objectively confirmed by imaging explorations with mandatory clinical and protective conditions.[40]

4. The national institute for public health of the Netherlands report recommended for prophylactic dose LMWH should be initiated in all hospitalized patients with COVID-19 irrespective of risk scores. COVID-19 patients with high clinical suspicion for PE, CT pulmonary angiography should be considered if the D-dimer level is elevated. The D-dimer threshold used should follow locally used algorithms. If PE is confirmed, therapeutic anticoagulation is indicated. They also recommended for hospitalized COVID-19 patients, routine D-dimer testing on admission and serially during hospital stay should be considered for prognostic stratification with additional imaging as available at local level.[12]

Till date COVOD-19 is considered as a respiratory system predominant disease. However recent studies with an understanding of etio-pathogenesis and atypical clinical manifestation lead us to understand the multisystem involvement. Here we have discussed and reviewed the coagulation system involvement in this disease. The different coagulation abnormalities frequently seen in COVID-19 infection are DIC, thromboembolism, thrombocytopenia and increased D-dimer. Our finding and suggestion for early diagnosis and treatment of abnormal coagulation in COVID infection are:

1. The coagulation abnormalities are slightly different from those seen in sepsis like combination of thrombocytopenia, prolonged prothrombin time, and increased D-dimer is suggestive DIC in COVID infection.
2. The thrombocytopenia is usually mild form with hardly less than 1lkh/ul. D-dimer is profoundly raised in severe disease and elevated D-dimer levels have poor prognostic factor.
3. Severe disease and ICU admitted patients should routinely screen for coagulation abnormality with D-dimer, platelet count and PT daily or alternate day.
4. A clinically suspected case of VTE and PE should go for early dropper ultrasound of limbs and CT angiography without delay with proper protective conditions.
5. Prophylaxis treatment with LMWH should start in all severely ill and ICU admitted patients in absence of contraindication.

CONCLUSION:

COVID-19 infection is multi-systemic disease. The coagulation abnormalities are commonly seen in this disease. As per recent studies from different parts of world, VTE and DIC are frequently reported coagulation abnormalities.. DIC is slightly different than the one seen in sepsis. Increased level of D-dimer is a common and the elevated level associated with poor prognosis and high mortality.

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