
Abstract
Coronavirus Disease (COVID-19) has presented significant challenges and burden to healthcare. Majority of patients have mild-moderate disease and are managed in a non-hospitalized home care setting by family physicians. COVID has pathological mechanisms that include endothelial injury and hypercoagulability due inflammatory mediators. COVID has shown to increase the risk of thromboembolism in hospitalized patients with severe disease and especially those in intensive care, and therefore D-dimer testing on admission and initiation of anticoagulant medication form an important part of hospital-based treatment. However, there is still little evidence suggesting an increased risk of thrombosis in mild-moderate non-hospitalized COVID patients who are not immobilized. Ordering a multitude of investigations including D-dimer in home isolated patients may sometimes affect clinical decisions, as D-dimer may be raised non-specifically due to inflammation. Currently routine D-dimer screening and anticoagulation is not recommended in non-hospitalized patients. In immobilized homecare COVID patients with multiple risk factors for thrombosis, a D-dimer may be done and an appropriate decision to start a direct-acting oral anticoagulant like apixaban may be taken. Apixaban can cause bleeding mostly non-major and rarely major. Patient should be well advised to be alert and timely report the same.

Keywords: Thrombosis; COVID; DOACs; Bleeding; D-dimer.

Introduction
Coronavirus disease (COVID-19 caused by SARS-CoV-2) has presented with diverse signs and symptoms, clinical decision challenges, and a significant burden on healthcare workers and infrastructure. It is known that >90% have mild symptoms and maintained oxygen saturation, therefore can be managed effectively with isolation and care at home or COVID basic repurposed isolation and care centers [1]. For such majority of patients, the Family Physicians (FPs) are the foundation of the community healthcare system to tackle the pandemic. Evolution of digital healthcare has further empowered patients and FPs towards meticulous monitoring and management of COVID.

COVID though initially regarded as primarily a viral respiratory disease affecting the airway and lungs, during the course of the pandemic further research suggested endothelial injury and systemic inflammation as part of its pathology [2]. The well-known Virchow’s triad implicates endothelial injury, and a hypercoagulable state (due to inflammatory mediators stimulating the coagulation cascade), and immobilization (as seen in hospitalized patients) contributing to stasis, as the factors leading to thrombosis. D-dimer levels in blood is a known marker for thrombosis in the presence of such risk factors, and this test is recommended to predict risk of thrombosis, poor patient outcomes and mortality in hospitalized and Intensive Care Unit
(ICU) patients [3,4]. Anticoagulation therapy is also recommend-
ed in hospitalized COVID patients as a significant component of
treatment. However, thrombosis risk in non-hospitalized, mild
COVID cases in homecare who are not immobilized, has not
been ascertained, and there is no confirmed recommendation
or established use of assessing D-dimer in these patients or giv-
ing Direct-Acting Oral Anticoagulants (DOACs) [5,6].

Case presentation

A 75-year-old male patient sought a digital consultation
with family physician for symptoms of fever of 101 °F for past
1-day, sore throat, weakness, and decreased smell and taste.
An RT-PCR was immediately recommended along with 4 hourly
monitoring of temperature and oxygen saturation (by pulse ox-
imetry). The RT-PCR was positive for COVID, with a Cycle Time
(Ct) of 24. Oxygen saturation was maintained ≥95%, therefore
the patient was treated in home isolation and care. Patient had
history of hypertension controlled on telmisartan 40 mg once
daily. Patient had no other comorbidities. A baseline blood test
(done on day 3) with Complete Blood Counts (CBC), C-Reactive
Protein (CRP) and blood sugar was within normal limits, and pa-
tient was advised to repeat the same on day 8.

Patient was asked to continue telmisartan and vitamin sup-
plements that he was already taking, and was also started on
paracetamol 6 hourly, povidone-iodine gargling twice daily, and
ivermectin once daily for 5 days (in accordance with national
protocol) [7]. Daily sharing with family physician of 4 hourly ox-
ycgen saturation and temperature charts was instructed, along
with advice given for twice daily conscious proning with inter-
mittent deep breathing, and once daily 6-minute walk test to
exclude subclinical hypoxia. The patient was to immediately re-
port oxygen saturation drop <95%. He was also advised on diet,
physical activity, rest and hygiene.

The patient decided to also take an opinion from his car-
diologist, who recommended additional blood tests of serum
creatinine, lipid profile, and inflammatory markers including
D-dimer. This was performed on day 5 and D-dimer was seen to
be 1000 mcg/L with serum creatinine and lipid profile within
normal limits. The patient was started on apixaban 2.5 mg
twice daily. On day 8 (2nd week of Illness), patient was symp-
tomatically improved with fever <100 °F and oxygen saturation
maintained ≥95% at all times. Blood tests were repeated that
showed a Neutrophil-Lymphocyte Ratio (NLR) of 4, D-dimer
of 1050 mcg/L, and CRP of 22 mg/L. Blood sugar and platelet
counts were normal. Patient was advised by FP for no further
medication, to continue oxygen saturation monitoring, and com-
plete the 2-week isolation period. However, the cardiolo-
gist advised to continue apixaban for a total of 4 weeks.

Patient repeated RT-PCR on his own on day 14, which was
negative. At 3 weeks, the patient presented with a dark red
patch at the upper back of his neck. The patch was macular
(flat) with irregular borders and there were no accompanying
symptoms like itching, pain, burning sensation, irritation or ul-
ceration. There was also no history of trauma. The patch was
discovered incidentally by his care giver while starting to give
him a hair trim (Figure 1). Clinical examination was suggestive of
a subcutaneous bleed. Patient had been on apixaban for almost
3 weeks at this time. Patient was investigated with CBC, CRP,
D-dimer and prothrombin time (INR). CBC parameters including
platelet count were in normal range. CRP was 9 mg/L, D-dimer
was 700 mcg/L, and PT-INR was 1.2. Apixaban was withdrawn,
and patient put on observation. The patch lightened in a week
and resolved completely within 10 days without any treatment
or intervention. Patient was asked to follow up for any post-
COVID symptoms for 3 months and advised to take first dose of
COVID vaccination there after.

Discussion

The incidence of thrombosis in COVID patients in the hospi-
tal setting has seen to be as follows: Venous Thromboem-
bolism (VTE) 28% and 10% in ICU and non-ICU patients respec-
tively; Arterial Thromboembolism (ATE) 3-5% and 2% in ICU and
non-ICU patients respectively [8]. Overall deep vein thrombosis
rate was 20-28% and pulmonary embolism rate was 13-19%
(both higher in ICU vs non-ICU patients). Mortality rate in hos-
pitalized COVID patients was 23% (in those with thromboembo-
lish) and 13% (without thrombosis) suggesting more than 70%
higher mortality rate if thrombosis develops [9]. A 4-fold rise
in D-dimer on admission (>2000 µg/L) could effectively predict
in-hospital mortality [3]. Therefore D-dimer tests on hospital
admission and during treatment monitoring, and starting pro-
phylactic anticoagulants in hospital setting is recommended.

However, the risk of thrombosis in non-hospitalized COVID
patients is not known [10]. There have been isolated case re-
ports of patients presenting with episodes of pulmonary em-
bolism, stroke and myocardial infarction weeks to months post
homecare and recovery from COVID [11]. However a retro-
pective study in 220588 patients suggested that 30 day post-
COVID VTE incidence outside of the hospital is not significantly
increased with SARS-CoV-2 infection and therefore suggesting
an absence of need for routine use of outpatient thrombopro-
phyaxis outside of clinical trials [12].

D-dimer can be elevated non-specifically in infections and
inflammation as would be seen in several COVID patients [13].
Also age corrected D-dimer in elderly (10 µg/L x age) should
be taken as cut off which in this case would be 750 mcg/L [14].
Therefore, doing D-dimer tests in homecare patients with mild-mod-
erate COVID who are not immobile may cause anxiety, affect
clinical decisions, and lead to many more patients receiving
DOACs than required. D-dimer testing and initiating anticoagu-
lation may be justified in homecare COVID patients with signif-
icannt risk factors like past history of thrombotic events, immo-
bility, multiple CVD risk factors or past intervention/procedures,
cancer, and kidney, liver or heart failure.
Apixaban shows a rate of non-major bleeds of 5-6/100 patient years and major bleeding rate of 1.5-2 (0.5 for intracranial hemorrhage)/100 patient years [15]. Non major bleeds include subcutaneous bleeds, epistaxis, hematuria, hemoptysis and gastro-intestinal bleeding. Most of these non-major bleeds show spontaneous resolution on drug cessation. The patient should be counselled and explained about timely reporting these adverse drug events.

**Conclusion**

COVID patients with mild-moderate symptoms who are physically mobile and managed in home care are at low risk for thrombosis that is similar to the general population. D-dimer test may show elevated levels in COVID patients as a non-specific marker of inflammation. D-dimer testing routinely or starting direct-acting oral anticoagulants are not required in home care COVID patients unless significant multiple risk factors, past history of thrombosis, or immobilization is present. Apixaban is one of the effective DOACs with an established safety profile, but is still best initiated by a specialist. Apixaban rarely causes serious bleeding, however non-major bleeds are not uncommon but mostly resolve. The patient should be explained about the signs of such bleeding episodes and report them timely to the treating physician.

**References**