

Severity of Deep Vein Thrombosis in COVID Pandemic

Kaashvi Udhwani*, Apurva G. Shah**, Henil Jariwala*, Rushabh Jani*

Abstract

Aim : To study the severity and complication rates of deep vein thrombosis (DVT) during the covid pandemic as compared to a similar time frame before the pandemic. **Materials and methods:** A group of 80 patient diagnosed with deep vein thrombosis between April 2020 to November 2020 (Group A) were compared with a group of 80 patients diagnosed with deep vein thrombosis during the similar time frame in 2019 with respect to several parameters indicating the severity and complication rates of deep vein thrombosis. **Results:** Deep vein thrombosis has showed an increased severity since the onset of covid with higher number of patients presenting with acute compartment syndrome requiring surgical intervention and with more number of cases showing extensive venous thrombosis. Complication rate with regards to pulmonary embolism has also showed a rise relating to the rise in patients presenting with extensive DVT.

Key words : Covid, Deep vein thrombosis, Pulmonary embolism, Venous thromboembolism

Introduction:

On December 31, 2019, the World Health Organization was informed of a cluster of cases of pneumonia of unknown cause detected in Wuhan City, Hubei Province, China. The pneumonia was caused by a virus called severe acute respiratory syndrome corona virus 2 (SARS-Cov-2), which was later named corona virus infectious disease 2019 (COVID-19). Symptoms are similar to the common cold, most notably fever and dyspnea. Venous thromboembolism (VTE), a frequent cardiovascular and/or respiratory complication among hospitalized patients, is one of the known sequelae of the illness. Hospitalized COVID-19 patients are often elderly, immobile, and show signs of coagulopathy. Therefore, it is reasonable to assume a high incidence of VTE among these patients. Moreover, D-dimer values are observed to increase in patients with covid, which also points to a relation between

these two. In this study, the methods of diagnosis and treatment of VTE, as well as the potential mechanisms of increased risk for VTE during the illness have been discussed. The severity and complication rates of deep vein thrombosis in patients during the covid pandemic have been compared with a similar group of people and similar time frame before the pandemic.

Methods:

It was a retrospective observational study carried out at Civil Hospital, Ahmedabad. Two groups – Group A and Group B were defined. Group A consisted of 80 randomly selected patients diagnosed with deep vein thrombosis from April 2020 to November 2020. Group B consisted of 80 randomly selected patients diagnosed with DVT from April 2019 to November 2019. In both these groups, patients who presented to OPD/Emergency with clinical features suggestive of Deep Vein Thrombosis such as lower limb swelling and pain, and on Duplex Ultrasound, diagnosed to be due to deep venous thrombosis were included in the study.

* Resident,

** Professor and Head of Unit, Department of General Surgery, B.J Medical College, Civil Hospital, Ahmedabad, Gujarat, India.

Correspondence : Dr. Apurva G. Shah

E-mail : shahapurvag@gmail.com

Inclusion criteria:

1. All patients with Duplex ultrasound suggestive of lower limb deep vein thrombosis were included

Exclusion Criteria:

1. Patients with upper limb Deep vein thrombosis were excluded
2. Patients with only superficial vein thrombosis were excluded.

Investigations such as a complete blood count, PT-INR (Prothrombin time- international normalised ratio), APTT (activated partial thromboplastin time), Serum homocysteine levels, a local part x-ray, Duplex ultrasound for DVT, ultrasonography of abdomen and pelvis to look for proximal extension and 2D Echocardiography were done in all the cases. Patients who presented with acute compartment syndrome were taken for emergency fasciotomy. All patients in both groups were immobilized and started on intravenous heparin (5000IU 6hourly) with or without oral anticoagulants (Tablet warfarin 2mg HS or Tablet Acetrom 1 mg Hs) with close monitoring of APTT and INR. D-dimer was done in patients who showed symptoms of pulmonary thromboembolism such as breathlessness, chest pain with dizziness/excessive sweating/low oxygen saturation.

Results:

Out of the 80 patients studied in both - Group A and B, approximately 70% patients were above the age of 50 years with predominance in males (62%). Deep vein thrombosis was observed to be more common in left lower limb (73%) in both groups. It was observed to be unilateral in most cases (84%).

Group A: The cause of deep vein thrombosis was “Post operative immobilization or paralysis” in 35% cases, “Traumatic Injury” in 20% cases, “Post

pregnancy” in 3.75% cases and “undefined” in the rest of the cases(41.25%). Group B showed “Post operative immobilization or paralysis” to be the most common cause contributing 42.5% to the total number of cases, followed by “Traumatic injury” (20%), “post pregnancy” (2.5%) and “undefined” in 32.5% cases.

Investigation of choice was Duplex Ultrasonography for lower limb Deep vein thrombosis. As per duplex ultrasound report, Partial thrombosis was present in 23.75% cases of Group A and 42.5% cases of group B. Complete thrombosis was present in 76.25% cases of Group A and 57.5% cases of Group B. Additionally, duplex showed extension of venous thrombosis in iliac veins or inferior venacava in 57.5% cases(Group A) and 47.5% cases (Group B). In 42.5% cases (Group A) and 52.5% cases(Group B), thrombosis was limited to lower limb and there was no proximal extension.

In Group A, 64 out of 80 patients(80%) were managed conservatively by injectable heparin and other oral anticoagulants. 12 patients(15%) required operative intervention in the form of fasciotomy with or without debridement for compartment syndrome(venous gangrene) and skin changes. 4 out of 80 patients(5%) all of which showed proximal extension of thrombosis upto infrarenal ivc underwent IVC filter placement. In contrast, in Group B, 92.5% patients were managed conservatively, 5% patients were operated for compartment syndrome and 2.5% patients underwent IVC filter placement. Out of the patients managed conservatively in Group A (64), 50 patients(78%) were admitted for a duration of >1 week and rest were discharged in less than a week. In contrast, out of 74 patients who were treated conservatively in group B, only 30 patients(40.5%) required admission for more than 1 week, rest were discharged within 1 week of admission. One of the

Figure 1: Number of cases showing complete/partial thrombosis

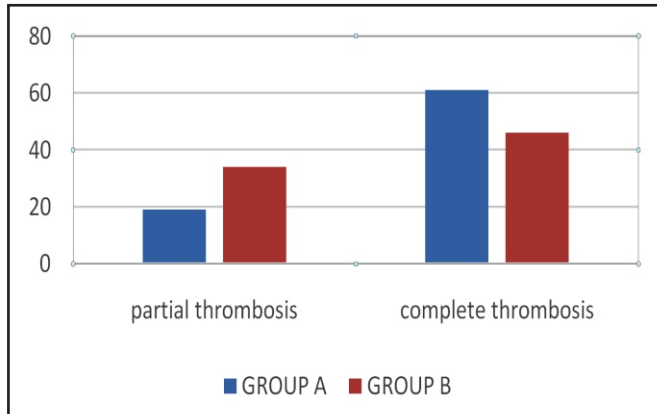


Figure 2: Percentage of total cases in each group with or without proximal extension

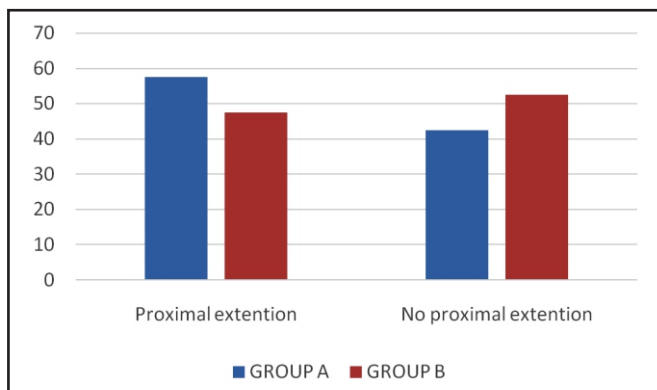
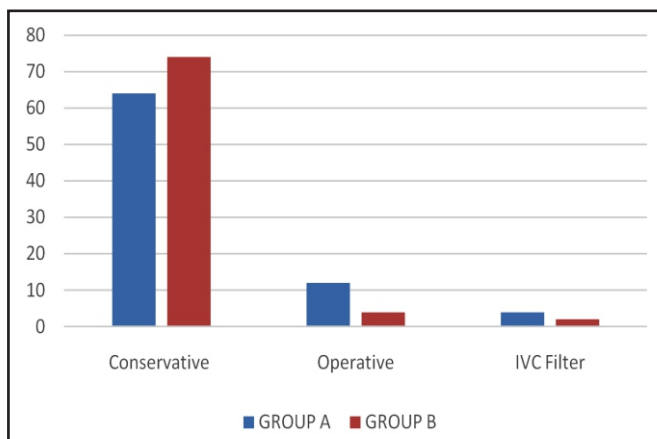
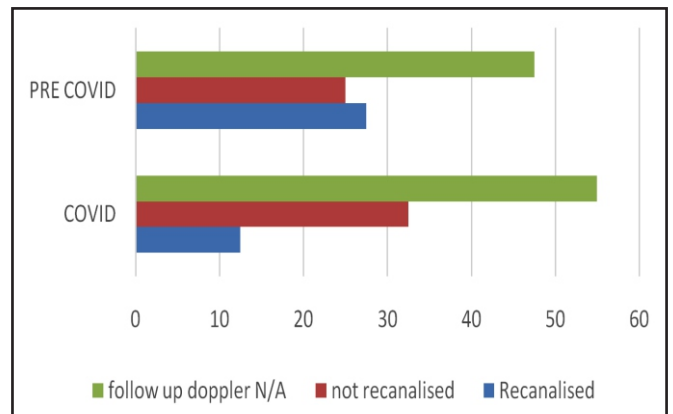


Figure 3: Percentage of patients requiring conservative/operative management for DVT



most dreaded complications of deep vein thrombosis is pulmonary venous thromboembolism, screening test for which is a “D dimer” assay. Out of 80 patients in Group A, 6 patients had an episode of pulmonary venous thromboembolism diagnosed

Figure 4: Recanalisation on follow up doppler*



* % of total cases

clinically and on the basis of d- dimer levels. All 6 patients required intensive care unit (ICU) management. Out of the 6 patients, 2 patient expired (mortality due to VTE out of 80 cases – 2.5%). In group B, 3 patients suffered from pulmonary venous thromboembolism out of which all required ICU care but there was no mortality. Total mortality (due to all causes) out of 80 cases in Group A was 5(6.25%). Total mortality in group B was 2.5%. Out of the 80 cases in Group A, 36 patients had undergone a follow up duplex ultrasound at 3 months, out of these 36, only 10 patients (27.7%) showed at least a partial recanalization, rest of the 26 patients did not show any recanalization. In contrast, in Group B, follow up Doppler was done in 42 patients out of which higher number of patients (22, 52.3%) showed at least a partial recanalization.

Discussion:

The COVID-19 pandemic started in December 2019 with a collection of patients presenting with pneumonia of unknown origin connected to a seafood wholesale market in Wuhan, China. Evidence, although limited, shows venous thromboembolism (VTE) as a complication of COVID-19. The exact mechanism of thrombus formation can be variable, but it is postulated that

COVID-19 can lead to an increase in the inflammatory response, hypoxia, immobilization, and disseminated intravascular coagulation (DIC), all of which can increase an individual's propensity to arterial and venous thromboembolic disease.

Mechanism of development of DVT: Viral infections, in general, can lead to an imbalance between pro- and anticoagulant states during the course of the disease and it often involves the disruption of the vascular endothelium. Various pathways involving the coagulation cascade, including elevated von Willebrand factor, cause the development of cross-linked fibrin clots. The breakdown of these clots leads to elevation of D-dimer levels and fibrin degradation product levels, both of which are associated with poor prognosis in COVID-19 patients, including the need for intensive care unit (ICU) admission, and even death. This activation of the systemic coagulation, along with immobility associated with bed rest, in COVID-19 patients increases the risk of VTE.⁽¹⁾

Difficulties in the Diagnosis of VTE in Patients with COVID-19⁽²⁾

Patients presenting with COVID-19 typically have a long course of disease, lasting up to several weeks.⁽³⁾ Some will need high oxygen supply and others will be intubated or treated with vasopressors. During this extended period of time, signs, symptoms and laboratory tests pointing to the diagnosis of VTE can be masked and attributed to COVID-19 or other complications occurring in the prolonged and sometimes complex hospitalization. D-dimer is increased in most of the patients, and usually cannot eliminate the presence of VTE. Therefore, timely diagnosis of VTE is anticipated to pose a significant challenge.

The clinical signs and symptoms of acute PE, the most menacing VTE event, are nonspecific.^(4,5) Some of the patients are asymptomatic and others have

dyspnea, chest pain, hemoptysis, presyncope or syncope, and up to hemodynamic instability. They can overlap with the symptoms of COVID-19 infection or its associated complications, such as Acute Respiratory Distress Syndrome (ARDS), pleural effusion, or myocarditis.⁽⁶⁻⁹⁾ Having one or more of the predisposing factors for VTE can be a clue to the diagnosis that otherwise can be missed. COVID-19 patients may have such factors at baseline or acquire them during their illness and hospitalization – older age, elevated CRP, D-dimer, fibrinogen levels, tachypnea, fever, critical illness, infectious etiology, and immobility. As for the diagnosis of DVT in COVID-19 patients, a low D-dimer level may help in ruling out the diagnosis. Nevertheless, most patients cannot be regarded as low probability risks, and if clinically suspected, compression ultrasonography is the method of choice, starting from proximal ultrasound and if negative performing whole-leg ultrasound with a sensitivity of 96–99% and specificity of 99.8% for lower-extremity DVT.⁽¹⁰⁾

Thrombophylaxis

A retrospective analysis of 449 COVID patients and 104 non-COVID patients in Tongji Hospital⁽¹¹⁾ showed that prophylactic anticoagulation therapy (40–60 mg enoxaparin per day or UFH 10,000–15,000 U/day) can reduce mortality, compared to those who do not receive it, only in the COVID group.

Another trial of the same group showed that heparin treatment for 7 days in 99 out of 449 patients⁽¹²⁾ with COVID-19 reduced 28-day mortality only in patients with a sepsis-induced coagulopathy score ≥ 4 (40% vs. 64.2%, $p = 0.029$) or patients with D-dimer >6 -fold of the upper limit of normal (32.8 vs. 54% $p = 0.017$). Finally, based on the correlation between high levels of D-dimer and severe COVID-19 disease as well as higher mortality rate, the International

Society on Thrombosis and Haemostasis (ISTH) and American Society of Hematology (ASH) guidelines⁽¹³⁾ advises prophylactic Low molecular weight heparin (LMWH) in all hospitalized COVID-19 patients in the absence of any contraindications (active bleeding and platelet count less than $25 \times 10^9/L$). In view of the high thromboembolic risk in patients with COVID-19 despite anticoagulation treatment, and in view of the thrombotic coagulopathy and extremely high D-dimers with no evidence of clinical bleeding in COVID-19 patients, some institute recommend considering higher prophylactic doses of anticoagulation such as enoxaparin 0.5 mg/kg b.i.d. or enoxaparin 1mg/kg once daily.

Conclusion:

Deep vein thrombosis has showed an increased severity since the onset of covid with higher number of patients presenting with acute compartment syndrome requiring surgical intervention and with more number of cases showing extensive venous thrombosis (complete and with proximal extension of thrombosis into major veins). An urgent fasciotomy has shown to be lifesaving in patients presenting with compartment syndrome (phlegmasia cerulea dolens). Most of the cases still showed recovery with conservative management but on follow up Doppler, we fail to observe even a partial recanalization of the venous thrombosis in most of the cases in the covid pandemic. Additionally, patients managed conservatively during the covid pandemic required a longer duration of admission. Complication rate with regards to pulmonary embolism has also showed a rise relating to the rise in patients presenting with extensive DVT. Intensive management of such patients is required to avoid and minimise mortality. Thromboprophylaxis by means of administration of LMWH in all hospitalised patients with covid positive status can go a long way in prevention of deep vein thrombosis and pulmonary thromboembolism.

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