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ORIGINAL ARTICLE

Using Pre-emptive Therapeutic Anticoagulation in Moderate to Severe Cases of COVID-19 is Associated with Improved Outcomes

MUHAMMAD ASIM RANA[1], MUJTABA HASAN SIDDIQUI[2], MOHAMMED REHAN OMAR SIDDIQUI[3], MUHAMMAD SOHAIL KHALID[4], WASEEM IQBAL[5], MOHAMMAD AHAD QAYYUM[6], RIZWAN PERVAIZ[7], MUHAMMAD FAISAL MUNIR[8], M. MUNEEB ULLAH SAIF[9]

[1]*Assistant Professor of Critical Care Medicine, Amna Inayat Medical College, Consultant Bahria International Hospital, Lahore, Pakistan*
[2]*Associate Professor of Medicine, Akhtar Saeed Medical and Dental College, Lahore, Pakistan*
[3]*Assistant Professor and Chief of Cardiology, United Medical and Dental College, Karachi, Pakistan*
[4]*Assistant Professor of Gastroenterology, Continental Medical College, Lahore, Pakistan*
[5]*Professor of Medicine, Vice Principal, Pakistan red Crescent Medical and Dental College, Lahore, Pakistan*
[6]*Assistant Professor of Nephrology, Amna Inayat Medical College, Consultant Bahria International Hospital, Lahore, Pakistan*
[7]*Senior Registrar Department of Critical Care Division of Medicine, Bahria International Hospital, Lahore, Pakistan*
[8,9]*Department of Critical Care Nursing, Division of Medicine, Bahria International Hospital, Lahore, Pakistan*
Correspondence to: Muhammad Asim Rana, Email: drasimrana@yahoo.com, Cell: 03435807006

ABSTRACT

Background: There is significant evidence to support that patients with the Coronavirus disease 2019 (COVID-19) have a higher propensity to develop thrombotic events. COVID-19 patients in intensive care units (ICU) have an increased rate of venous thromboembolism (VTE), ranging from 17% to 25%. Apart from acute respiratory failure, coagulopathy remains a common abnormality in these patients, within creased levels of both fibrinogen and D-dimers. Anticoagulation using subcutaneous heparin is known to reduce the incidence of thromboembolic events; although concern regarding over-anticoagulation resulting in excessive bleeding remains an impediment.

Objective:

Study Design: Retrospective study

Place and Duration of Study: Bahria International Hospital Lahore from 1st May 2020 to 31st October 2020.

Methodology: One hundred and eight patients admitted in the ICU were enrolled. The incidence of thrombotic and bleeding events in patients treated with subcutaneous heparin during their admission with moderate to severe COVID19 in the ICU. All patients were given therapeutic dosed anticoagulation universally unless contraindicated.

Results: Thromboembolic events were seen in 10 patients while 98 patients did not have any such event. 3 patients had a bleeding event during their stay.

Conclusions: Using prophylactic therapeutic dose anti-coagulation therapy is an effective and safe strategy in COVID-19 patients and it is associated with improved outcomes in terms of reducing morbidity and mortality.

Keywords: SARS-CoV-2, COVID-19, Thrombosis, D-Dimers, Hypercoagulability, Bleeding, Hemorrhagic event, Anticoagulation

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is known to cause acute respiratory distress due to novel coronavirus 2 (SARS-CoV-2) virus infection. Its impact on the respiratory system remains the main reason of its morbidity and mortality worldwide.[1] Over time the understanding behind this virus's aetiology and pathogenesis has evolved with significant evidence describing a tendency towards hypercoagulability in COVID-19 affected patients.[2] The thrombotic events are largely due to the disease progress activating multiple systemic inflammatory and coagulation responses that can result in various venous or arterial thromboses as complications of the contagion.

The current coronavirus disease 2019 pandemic has been a major reason for high intensive care unit (ICU) admission and high mortality since December 2019.[3] Recent studies have revealed that patient with COVID-19 are prone todevelopCOVID-19 patients in intensive care units (ICU) have an increased rate of venous thromboembolism (VTE), ranging from 17% to 25%. Other than acute respiratory failure, coagulopathy is the most common abnormality in patients with COVID-19, with increased levels of both fibrinogen and D-dimers.[4,5] Therefore, evidence supports the administration of prophylactic doses of low molecular weight heparin in all COVID-19 patients to prevent coagulopathy in COVID-19 patients.[6] Some centres have supported a therapeutic dose anticoagulation therapy in all COVID19 patients to alleviate the risk of pulmonary embolism.[7]

The main reason for not using high dose anti coagulation is higher risk of bleeding and intracranial hemorrhage. Different studies on oral anticoagulation described significant adverse effects in general. These patients had excessive bleeding and higher risk of mortality as compared to other patients.[8]

This study was carried out to look at the incidence of thrombotic or thromboembolic events (TE) as well as hemorrhagic events (HE) occurring in critically ill COVID-19 patients receiving therapeutic dose anticoagulation as a prophylaxis, admitted to Bahria International Hospital Lahore. Thromboembolic events consisted of myocardial Infarction (MI), deep vein thrombosis (DVT), thrombotic cerebrovascular events and pulmonary embolism. Whilst intracerebral bleeding, upper and lower gastrointestinal bleeding, haematuria and conjunctival haemorrhage were considered as a bleeding event. Our centre has full therapeutic anticoagulation protocol for all moderate to severely sick COVID-19 cases admitted to our High Dependency Unit (HDU) and Intensive Care Unit (ICU) except those who had contraindications.

MATERIALS AND METHODS

This is a single centre retrospective study wherein all COVID19 patients admitted at the Bahria International Hospital Lahore Medical ICU from 1st May 2020 till 30th July 2020 were included. All patients received full-dose therapeutic anticoagulation as a prophylaxis (Enoxaparin 1 mg per kg twice a day, subcutaneously). The incidence of thromboembolic and hemorrhagic events was noted and were considered the primary outcomes. Thromboembolic events consisted of Myocardial Infarction (MI), Deep Vein Thrombosis (DVT), thrombotic cerebrovascular events and pulmonary embolism. Whilst intracerebral bleeding, upper and lower gastrointestinal bleeding, hematuria and conjunctival hemorrhage were considered as a bleeding event.

Anticoagulant therapy comprised of Enoxaparin administered subcutaneously 1 mg per Kg twice a day. Any patient requiring admission to the Medical ICU due to COVID19 was considered to have a moderate to severe illness. Any patient having contraindications to anticoagulant administration was excluded from the study. The data was entered and analyzed through SPSS-25.

RESULTS

The mean age of the participants was 54 while 58% of the participants were male (Table 1). The mean platelet count was

271.41±98.15 10^9/L, similarly the mean of CRP, Serum LDH and D-Dimers respectively were 61.80±80.52 mg/L, 389.28±246.30 u/l and 572.89±386.11 u/l respectively (Table 2). Out of these patients' thromboembolic events were seen in 10 patients (9.25%) patients while 98(90.74%) patients were free from any type of thromboembolic event (Fig. 1). There were 3 patients who experienced a hemorrhagic event while 105 patients remained free from any hemorrhagic event. From amongst the 3 patients who experienced a bleeding event 2 had a gastrointestinal bleed while 1 had hematuria. No patient has an intracerebral bleed (Fig. 2).

Table 1: Demographic information of the patients (n=108)

Variable	No.	%
Gender		
Male	63	58.3
Female	45	41.7
Age (years)	53.7±4.28	

Table 2: Descriptive statistics of the patients

Laboratory test	Mean±SD
Platelet Count (10^9/L)	271.41±98.15
CRP (mg/L)	61.80±80.52
Serum LDH (u/l)	389.28±246.30
D-Dimers (ng/L)	572.89±386.11

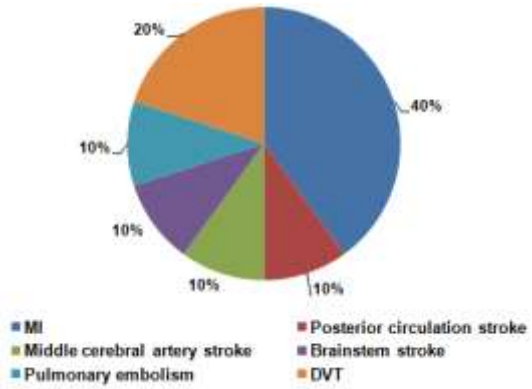

Fig 1: Figurative description of thromboembolic events

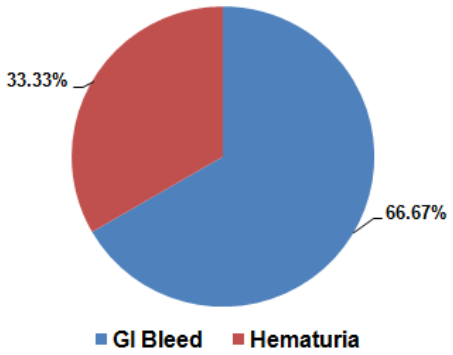

Fig 2: Figurative description of hemorrhagic events

DISCUSSION

Ever since the world has started combating COVID-19 there has been growing interest on anticoagulation because of increased thrombotic events in patients and various approaches has been introduced. We in the beginning were following D-dimers and escalating our anticoagulation from prophylactic to therapeutic (1 mg per kg of Enoxaparin or dose adjustment in case of kidney involvement but this approach was cumbersome as we had to get D-dimers daily and review doses daily which was adding a financial burden too. Our COVID-19 treatment and management board decided to go for therapeutic anticoagulation and a standard therapeutic dose regimen was adopted for adult moderate to severe disease patients admitted in Bahria International hospital. Considering the effects on immune-thrombogenesis or inflammation mediated coagulopathy we checked Platelets, CRP, LDH and D-dimers in all patients.

In the present study, thromboembolic events were seen in 10 patients (9.25%) patients while 98 (90.74%) patients were free from any type of thromboembolic event. Llitjos et al[10] conducted a similar study and described similar results.

The minimum average platelet count was 68(109/L), maximum average platelet count 745 (109/L) and the mean of total platelet count was 271.41 (109/L) with standard deviation 98.153. Similarly, the average mean of CRP, Serum LDH and D-Dimers respectively was 61.80 (mg/L), 389.28 (u/l) and 572.89(ng/L). Similar study conducted by Llitjos et al[10] showed that in COVID patients median D-dimer value was 1750 ng/mL, median CRP value was 187 mg/L, and median of Platelets count was 234(109/L).

It is to be noted that, in our study of 108 patients, Incidence of TE was only seen in n = 10 (9.25%) of the patients, while n = 98 (90.74%) did not experience any form of TE. These rates are considerably low in comparison to the rate of TE in critically ill patients documented in literature thus far, which have been 40% by Fraissé et al [11], and 69% in a study by Llitjos et al[10] who performed a systematic screening with doppler ultrasound. Both of above reference studies administered two types of doses of anticoagulants, standard (prophylactic) or full-dose (therapeutic) dose according to their risk factors for thrombosis but in our study, we gave only therapeutic dose to every patient. The results observed are encouraging, as they are almost 60% less than documented literature.

Our study's results of haemorrhage is less than those of a similar study conducted by Fraissé et al[11] which reported 21% rate of significant haemorrhage. In our study, we only had 3 patients with bleeding events and those were not life threatening.

CONCLUSION

The results of present study conclude that prophylactic anti-coagulant therapy in treatment dose is effective and safe in COVID-19 patients as it is associated with improved out comes in terms of lower incidence of thromboembolic events whilst hemorrhagic events were also minimal. This study suggests the use of therapeutic anti-coagulant treatment as a strategy for treating COVID-19 patients who fall in moderate to severe categories in hospital settings.

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