Current Trend of Prescribing Anticoagulant and Antiviral Drugs in the Treatment of COVID- 19 Patients in a Corona Dedicated Hospital in Khulna

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Abstract

Background: Thrombo-embolic incidence secondary to COVID-19 with increased mortality rate has become a global concern. Anticoagulants are widely used to prevent mortality. On the other hand, antiviral therapy has a potential effect against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). **Aims & objectives:** This study aims to assess the use pattern of anticoagulant and antiviral drugs against COVID-19. **Methods:** This is an observational cross-sectional study where two hundred COVID-19-positive patients of both sexes and different age groups who received anticoagulants and antivirals were recruited. All data were compiled in a Microsoft excel spreadsheet. Results were expressed in frequency & percentage. **Results:** Out of 200 patients, there were 115 males (57.5%) & 85 females (42.5%); the majority (56%) belonged to the age group between 30 to 60 years. Clinically, patients were categorized into mild (25%), moderate (32%), severe (37.5%), and critical (5.5%) cases. In this study, 88% of patients received low molecular weight heparin (enoxaparin) in a prophylactic dose and 12% of patients received in a therapeutic dose. Among the antivirals, remdesivir (84%) followed by favipiravir (16%) were the most commonly prescribed drugs. **Conclusion:** Anticoagulant (enoxaparin) and antiviral (remdesivir) drugs are frequently prescribed in the treatment of COVID-19 patients.

Keywords: Enoxaparin, Remdesivir, COVID-19

Introduction

The increased spread of the overwhelming number of cases of COVID-19 caused by SARS-CoV-2 (severe acute respiratory syndrome-corona virus-2) is a major global health crisis.[1,2] The symptoms caused by COVID-19 range from mild upper respiratory symptoms to multi-organ failure complicated by a severe hypercoagulable state with a high risk of venous thromboembolism[3] which has been associated with poor prognostic outcomes.[1,4] The severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is responsible for an intense systemic inflammatory syndrome and an endotheliopathy leading to coagulation activation.[5]

Some important factors like Inhibition of the plasminogen system, platelet dysfunction and complement activation in COVID-19 are responsible for the development of coagulopathy.[2]

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Patients who died of COVID-19 pneumonia showed significantly increased higher levels of D-dimer and fibrin degradation products (FDP), longer prothrombin time (PT), etc.[6]

Unfractionated heparin (UFH) and low-molecular-weight heparin (LMWH), seemingly important to reduce fibrin deposition, microthrombi formation and prothrombotic state in the patients, act by promoting the formation of an intermediate protease–heparin–antithrombin complex which facilitates inhibition of thrombin and activated factor X.[2,6] The administration of low molecular weight heparin (LMWH) at prophylactic dose is highly recommended for all hospitalized patients with COVID-19 infection. Patients who appeared to be associated with lower mortality rates and improved prognoses received LMWH compared to those without LMWH.[3,6-10]

Without any proven effective therapy, many patients have received compassionate-use therapies, including antiretrovirals, antiparasitic agents, anti-inflammatory compounds, and convalescent plasma.[11] Currently, remdesivir is a promising potential therapy for COVID-19 due to its broad spectrum of activity against members of several virus families, including filoviruses (e.g., Ebola) and coronaviruses (e.g., SARS-CoV and Middle East respiratory syndrome coronavirus [MERSCoV]) that inhibits viral RNA polymerases.[11-13]

The current dose under investigation is a single 200-mg intravenous (IV) dose on day 1 followed by 100-mg IV daily for up to 10 days, infused over 30-60 min.[13,14] Dose adjustments initially are not recommended in patients with an estimated glomerular filtration rate of less than 30 ml/min.[13] Clinical trials are ongoing to evaluate the safety and antiviral activity of remdesivir in patients with COVID-19.

As our healthcare system observed a decline in COVID-19-related mortality during the end of the second wave of the pandemic in our country, we sought to explore the impact of different medication combinations on mortality. We examined the impact of changing practice patterns in the treatment of COVID-19 with various treatments including anticoagulants, antivirals, etc.

Materials and methods

This study was a prospective cross-sectional study conducted on two hundred (200) COVID-19-positive patients admitted to the corona unit of Gazi Medical College & Hospital (GMCH), Khulna over four months from May 2021 to August 2021. Consenting adult patients aged>18 years of both sexes who presented with co-morbidities and received anticoagulants & antivirals were included in the study; pregnant women, and patients who received treatment without anticoagulant & antiviral drugs were excluded from the study. Ethical approval was obtained from the Institutional Review Board of GMCH and informed written consent was also obtained from each patient before recruitment. A specially designed questionnaire was used to record the participants' demographic profiles. The severity of the disease was categorized as mild, moderate, severe, & critical cases by following our national guidelines. Patients who received anticoagulants (Enoxaparin) were divided into two groups as per national treatment protocol; prophylactic group [Enoxaparin 40 mg, subcutaneously (SC), once daily] and therapeutic group [Enoxaparin 1mg/kg, SC, twice daily]. After collecting all the information required for the study, data were compiled in the form of tables & figures by using an MS Excel spreadsheet and the result was expressed in percentages.

Results

A total of 200 COVID-19-positive patients who started antiviral & low molecular weight heparin (LMWH) from the day of admission to the hospital were included in the study. Male patients [115 (57.5%)] were more than female patients [85 (42.5%)]. The majority of them were in the age group between 30 to 60 years [112 (56%)]. Diabetes mellitus (DM) was the most common coexisting disease [68 (34%)] followed by hypertension [60 (30%)], ischemic heart disease [45 (22.5%)], bronchial asthma [15 (7.5%)], COPD [09 (4.5%)]

and chronic renal disease [03 (1.5%)]. All these characteristics of the study population at admission are shown in Table 01.

Table 01: Demographic characteristics of the study subjects

Characteristics of the study subjects		Total number n=200	Percentage (%)
Age (years)	<30	26	13%
	30-60	112	56%
	>60	62	31%
Gender	Male	115	57.5%
	Female	85	42.5%
Co-morbidities	Diabetes	68	34%
	Hypertension	60	30%
	Ischemic heart disease	45	22.5%
	Bronchial asthma	15	7.5%
	COPD	9	4.5%
	Chronic renal disease	3	1.5%

Clinical signs/symptoms of different categories (mild, moderate, severe & critical) are shown in Table 02 where the severity margin of the patient is identified by following our national guidelines.

Table 02: Severity margin of the patients according to the national guidelines of Bangladesh

a) Mild cases
• The clinical symptoms are mild, and there is no sign of pneumonia on imaging.
• Symptoms may be: fever, cough, sore throat, malaise, headache, muscle pain without shortness of breath or abnormal imaging
b) Moderate cases
• Adolescent or adult with clinical signs of pneumonia (fever, cough, dyspnoea, fast breathing) but no signs of severe pneumonia.
• Respiratory distress with < 30 breaths /min
• Pulse oxymetry showing saturation > 90% at ambient air
c) Severe cases
cases meeting any of the following criteria:
• Respiratory distress (≧30 breaths/ min)

• Finger oxygen saturation ≤ 90% at rest
• Arterial partial pressure of oxygen (PaO2)/fraction of inspired oxygen (FiO2)≦300mmHg (1mmHg=0.133kPa)

d) Critical cases
cases meeting any of the following criteria
• Respiratory failure and requiring mechanical ventilation
• Shock
• With other organ failures that require ICU care.

Out of 200 patients, mild cases were 50 (25%), moderate cases were 64 (32%), severe cases were 75 (37.5%) and critical cases were 11 (5.5%) who received LMWH (enoxaparin) and antivirals. These findings are shown in Figure 01.
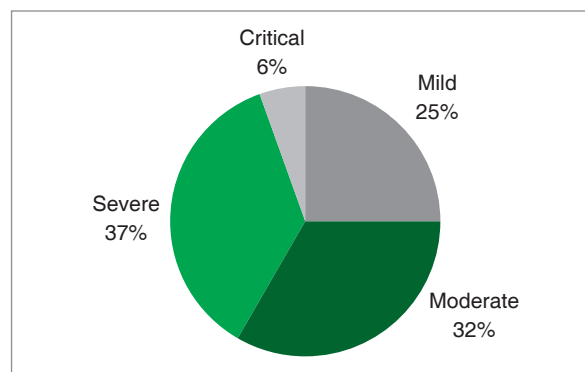

Figure 01: Distribution of the patients in different clinical categories

Total of 176 (88%) patients received LMWH in prophylactic dose whereas only 24 (12%) patients received the drug in therapeutic dose are shown in Figure 02. The dose was maintained according to national treatment guidelines.
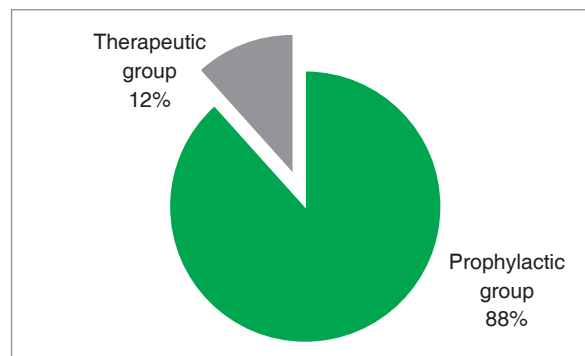

Figure 02: Distribution of the patients receiving anticoagulant (Enoxaparin)

The distribution of patients in different clinical categories who received antiviral drugs is shown in Figure 03. The most commonly prescribed antiviral drug was remdesivir 168 (84%) followed by favipiravir 32 (16%). Favipiravir was used in mild (40%) & moderate (18.75%) cases only. All severe (100%) & critical (100%) cases received remdesivir and side by side mild 30 (60%) & moderate 52 (81.25%) cases also. All these findings are shown in Figure 03.
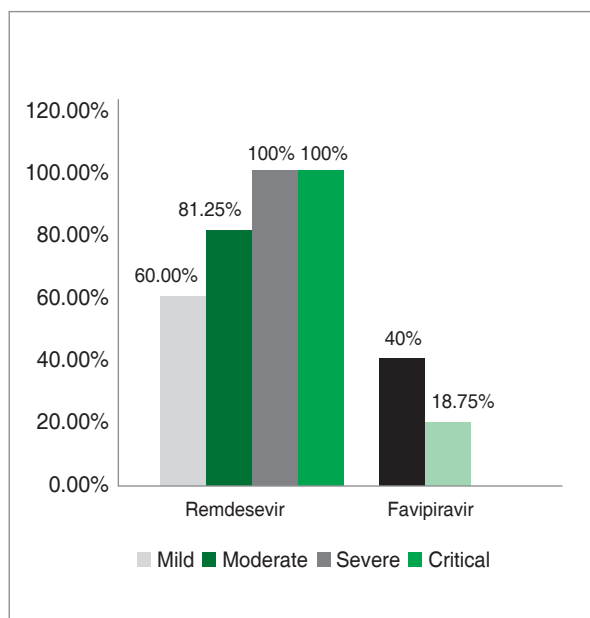

Figure 03: Distribution of patients receiving antiviral drugs

Discussion

This is an observational prospective study where a total of 200 patients receiving antiviral drugs and anticoagulants were enrolled. Male patients (57.5%) were more commonly prescribed those drugs than female patients (42.5%). This is consistent with some other studies.[5,8,9,11,13,15,16-18] Most of the patients [112 (56%)] were in the age group ranging between 30 to 60 years. Similar findings were found in a study conducted by Arslan et al.[19] But it differs from other studies done by Helms et al., Coppock et al., Grein et al., Arnold et al., Y. Cen et al., etc where most of the patients were in >60 years age group.[5,9,11,17,20]

Recruited patients had higher rates of pre-existing co-morbidities, such as diabetes 68 (34%), hypertension 60 (30%), ischemic heart diseases 45 (22.5%), bronchial asthma 15 (7.5%), etc. It is in concordance with other studies conducted by Helms et al., Moonla et al., Grein et al., Tassiopoulos et al., Arnold et al., Beigel et al.[5,8,11,15,17,18] Clinical categories of the patients were divided into four groups (mild, moderate, severe & critical) based on severity by following our national guideline. The number of patients in different categories was: mild 50 (25%), moderate 64 (32%), severe 75 (37.5%) and critical 11 (5.5%). Patients were managed following our current guidelines.

LMWH (enoxaparin): most of the patients [176 (88%)] received enoxaparin at prophylactic doses and in some severe and critical cases [24 (12%)] received it at therapeutic doses. Other studies have shown similar findings where the prophylactic dose is prescribed more than the therapeutic dose. Some other studies also revealed the dose category of enoxaparin.[1,5,6,8,10,21,22] As mild cases present with co-morbidities so enoxaparin is indicated in those cases.

Antivirals (remdesivir, favipiravir): antiviral drugs were frequently prescribed during our study period. Remdesivir [168 (84%)] and favipiravir [32 (16%)] were given to the patients in different categories. Mild (60%), moderate (81.25%), severe (100%) & critical (100%) cases received remdesivir. The use of remdesivir in the treatment of COVID-19 is very common in other countries.[11,12,14,18,30-34] In this study, favipiravir was used in mild (40%) & moderate (18.75%) cases only. Pilkington et al. showed patients treated with favipiravir had a beneficial effect.[23] Some other studies also revealed the beneficial effects of favipiravir.[13,24-28] Besides remdesivir and favipiravir, other antiviral drugs like oseltamivir, lopinavir, ritonavir, ribavirin, umifenovir, are used in other countries.[13,29]

Our study had some limitations. First, not all laboratory tests were performed on all patients,

so our study could not document the disease progression. Besides, a follow-up of 28 days was not done which might cover all the disease stages. The adverse effects of these two categories of the drug were not monitored. A further study is recommended to assess the efficacy of the drugs prescribed to the patients and also intensive monitoring should be done for possible adverse events.

Conclusion

As our study aimed to assess the use of anticoagulants and antivirals, we found remdesivir as antiviral and enoxaparin as anticoagulant being the frequently prescribed drugs along with other supportive drugs to fight against different clinical categories of COVID-19 patients.

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