The outcome of early treatment with Rivaroxaban among a sample of COVID-19 patients: A cross-sectional study

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The outcome of early treatment with Rivaroxaban among a sample of COVID-19 patients: A cross-sectional study

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ABSTRACT

Background. COVID-19 is considered a prothrombotic disease. According to this established hypercoagulable state associated with increased COVID-19 mortality and morbidity, a focus on antithrombotic treatment was developed. Literature reported that anticoagulants and antithrombotic treatment were beneficial in reducing COVID-19 morbidity and mortality. Rivaroxaban is one of the treatments under study.

Purpose. To assess the effectiveness of early administration of Rivaroxaban in reducing COVID-19 mortality.

Method. A cross-sectional analytical study was conducted among 437 Iraqi patients with COVID-19. The patients visited an outpatient consultation clinic, and the data were collected over a period extending from February 2021 to the end of December 2021. All patients who had received Rivaroxaban 20mg 1x1 as early treatment, irrespective of their D. dimer level or COVID-19 severity, were included in the study.

Results. The total study sample was 437 COVID-19 cases with a mean age of (56 ± 20 years). Of most study patients, 315 (80.3%) had moderate COVID-19. Patients of our sample who used Rivaroxaban as an anticoagulant and needed ICU admission were 26 (5.9%). Only 5 cases (1.1%) have died.

Conclusion. Rivaroxaban 20 mg 1×1 as early treatment in moderate and severe COVID-19 cases can provide potential protection from thrombotic events.

Keywords: Rivaroxaban, COVID-19, anticoagulants, D-dimer, Ibn-Sina Hospital, thrombotic diseases

Introduction

COVID-19 is considered a prothrombotic disease. Many hypotheses have been developed to explore the causes of coagulation abnormalities. It is thought that endothelial vascular injury observed in COVID-19 tied with coagulopathic pathways causes thrombotic complications, including arterial, venous thromboembolic, and in-situ arterial microthrombi [1,2]. It is undecided if this endothelial damage occurs because of the direct effect of SARS-CoV-2 or indirectly by the cytokine storm, or by a combination of mechanisms [3].

In addition, thrombosis, disseminated intravascular coagulation, and cytokine storm has been associated with worse COVID-19 severity and outcomes [4]. Previous studies reported that around 25% of patients with COVID-19 admitted to the intensive care unit are expected to develop thrombotic complications [5-7]. The life-threatening thrombotic events in COVID-19 are microvascular thrombosis, possibly the causative of diffuse lung injury seen in patients with COVID-19 [8]. The major causes of mortality in COVID-19 are progressive hypoxemic respiratory failure and ARDS; this happens because of the viral invasion of the lung alveoli activated by the cytokines storm associated with the activation of thrombosis, which leads to microvascular and macrovascular thrombosis with diffuse lung injury [9].

According to this established hypercoagulable state associated with increased COVID-19 mortality and morbidity, focusing on antithrombotic treatment was developed [10]. The previous review suggested that prophylactic anticoagulants were safe and effective for hospitalised patients with COVID-19 [11]. Literature reported that anticoagulants and antithrombotic treatment were beneficial in reducing COVID-19 morbidity and mortality [12-14]. Rivaroxaban is an oral selective factor Xa inhibitor with high bioavailability ranging (from 80-100%) for the 10 mg tablet irrespective of food intake and for the 15- and 20 mg tablets when taken with food [15].

The study aimed to assess the effectiveness of early administration of Rivaroxaban 20 mg 1x1 among moderate and severe COVID-19.

Methods

A cross-sectional analytical study was conducted among 437 Iraqi patients with COVID-19. The patients visited a private outpatient consultation clinic, and the data were collected over a period extending from February 2021 to the end of December 2021.

All patients with moderate and severe COVID-19 who had received Rivaroxaban 20mg 1×1 as early treatment, irrespective of their D. dimer level or COVID-19 severity, were included in the study.

Inclusion criteria

- Age > 18 years.
- A positive PCR test confirmed COVID-19 diagnosis.
- Moderate and severe COVID-19 cases.

Exclusion criteria

- Patients with haemolytic diseases.
- Patients on antithrombotic medications rather than Rivaroxaban.
- Patients with a history of haemorrhagic CVA.
- Patients with a history of GIT ulcers.
- Pregnant women.
- Females with fibroids, menorrhagia, or any gynaecological condition combined with vaginal bleeding.

The sample size was selected conveniently as all the positive COVID-19 with moderate and severe severity fulfilled the inclusion criteria and signed an informed consent to accept to use of their data in the study. The data were collected using a structured data collection form. The data were age, sex, smoking history, BMI, DM, HT, IHD, history of lung disease, the severity of COVID-19, D. dimer level, treatment with Rivaroxaban, outcome, thrombotic events, and the occurrence of bleeding. All patients were followed up till full recovery or death occurred. The recovery was considered when the fever fully subsided, the returned normal SpO2 level to normal, and the returned D. dimer level to normal.

Verbal consent was taken from all the patients or their relatives for using the data after explaining the aim of the study to the researcher. Complete confidentiality was ensured, and the data were collected with serial ID without an identity and for research purposes only.

Statistical Analysis

Data were introduced into Microsoft Excel 365 and loaded into SPSS (Statistical Package for Social Sciences) version-26. Parametric data are presented as mean and standard deviation.

Categorical data are presented as numbers and percentages.

The chi-square test and Fisher exact test were used to test homogeneity. P-value < 0.05 was considered as discrimination of significance.

Results

The total study sample was 437 COVID-19 cases with a mean age of (56 ± 20 years). The highest proportion, 21.1% (91 cases) within the age group > 75 years. Females contributed to the highest proportion, 60.0% (262 cases). Smokers were 90 cases (20.6%). Patients with diabetes mellitus were 99 (22.7%); and with hypertension were 137 (31.4%), and with ischemic heart disease were 92 (21.1%). As shown in Table 1.

Table 1: Demographic characteristics of the study sample

Variables		Mean ± SD /No. (%)
Age (years) / **range**		**56 ±20 years (20 - 90)**
BMI		**30 ± 6 kg/m^2**
Age group (In years)	**20 – 35**	88 (20.1)
	36 – 45	63 (14.4)
	46 – 55	71 (16.2)
	56 – 65	50 (11.4)
	66 – 75	73 (16.7)
	> 75	92 (21.1)
Gender	**Female**	262 (60)
	Male	175 (40)
Smoking History	**No**	347 (79.4%)
	Yes	90 (20.6)
Diabetes Mellitus	**No**	338 (77.3)
	Yes	99 (22.7)
Hypertension	**No**	300 (68.6)
	Yes	137 (31.4)
Ischemic Heart Disease	**No**	345 (78.9)
	Yes	92 (21.1)

Of most study patients, 315 (80.3%) had moderate COVID-19. D- dimer was elevated in 358 (81.9%). Hospitalized patients were 86 (19.7%). Patients who needed ICU admission were 26 (5.9%). Only 5 cases (1.1%) have died. Clinical bleeding (including menorrhagia, epistaxis, and bleeding gingivitis) occurred among 34 (7.8%). Most cases with clinical bleeding were females 55 (64.7%), and most were with menorrhagia 20 (58.8%), as shown in Table 2, Figure 1.

Table 2: COVID-19 clinical characteristics of the study sample

Variable		No. (%)
COVID- 19 severity	**Moderate**	351 (80.3)
	Severe	86 (19.7)
D-dimer level	**Elevated > 500 ng/ml**	358 (81.9)
	Normal ≤ 500 ng/ml	79 (18.1)
Hospitalization	**No**	351 (80.3)
	Yes	86 (19.7)
ICU admission	**No**	**411 (94.1)**
	Yes	**26 (5.9)**
Outcome	**Recovered**	432 (98.9)
	Died	5 (1.1)
Clinical bleeding	**No**	403 (92.2%)
	Yes	34 (7.8%)

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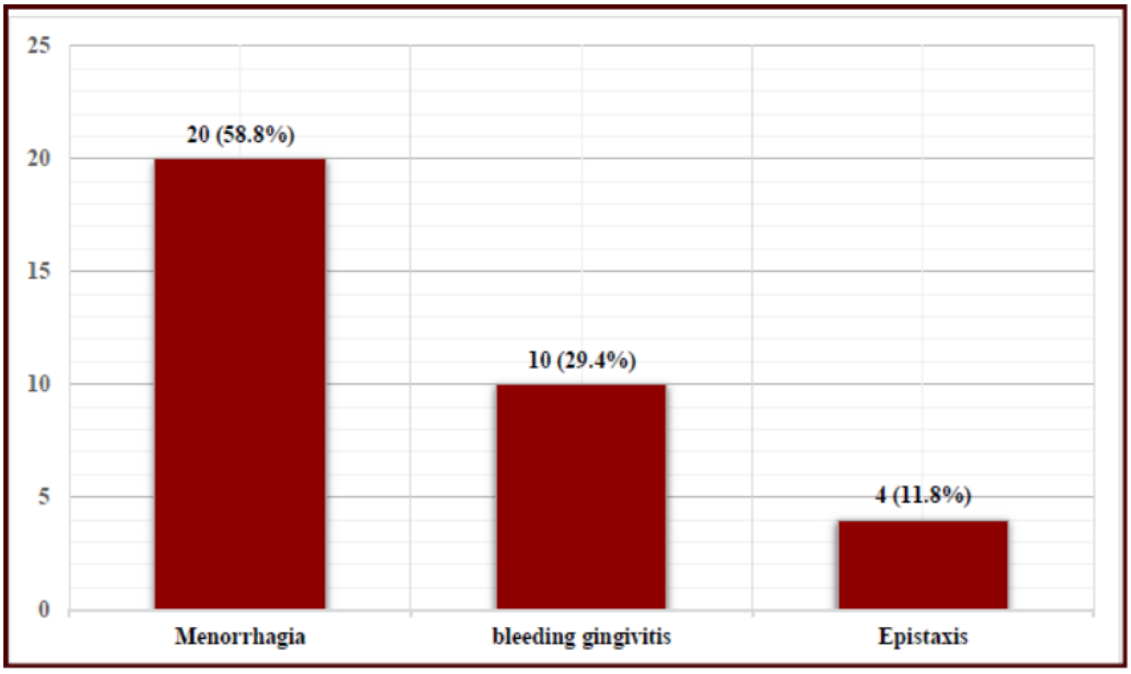

Figure 1: Distribution of bleeding tendency among study sample.

Table 3: Distribution of D. Dimer level among the study sample

Variables		D. Dimer level				P-value
		Normal ≤ 500 ng/ml		**Elevated > 500 ng/ml**		
		No.	**%**	**No.**	**%**	
Age group (In years)	**20 – 35**	**13**	**14.8**	75	85.2	0.727
	36 – 45	**15**	**23.8**	48	76.2	
	46 – 55	**12**	**16.9**	59	83.1	
	56 – 65	**10**	**20**	40	80.8	
	66 – 75	**11**	**15.1**	62	84.9	
	> 75	**18**	**19.6**	74	80.4	
Gender	**Female**	**50**	**19.1**	212	80.9	0.504

	Male	**29**	**16.6**	146	83.4	
Covid-19 severity	**Moderate**	**70**	**19.9**	281	80.1	0.041
	Severe	**9**	**10.5**	77	89.5	

The clinical characteristics of the five dead cases from the study sample were illustrated in table 4.

Table 4: Medical history of the study died cases.

Case	Demography	Past medical history	D-dimer in ng/ml	Evidence of bleeding	Evidence of marcrovascular thrombosis
1.	37 years, male	DM, smoker	1887	No	No
2.	45 years, female	HT, IHD and DM	1990	No	No
3.	78 years, male	HT, obesity	1760	No	No
4.	75 year, male	HT, IHD and DM	1995	No	No
5.	90 year, male	DM	1999	No	No

Discussion

Rivaroxaban is established to reduce venous and arterial thrombotic events risk in various indications [16-21]. A previous study conducted among patients with different infectious diseases found that prolonged prophylaxis with rivaroxaban reduced thrombotic events in patients, especially those admitted for active lung infections. Efficacy benefits were, in part, offset by bleeding outcomes [21]. A study by Capell et al. [22] concluded that factor Xa has a potential role in the pathogenesis of coronavirus morbidity and mortality. Moreover, outpatients and hospitalised COVID-19 patients could benefit from early prophylaxis with rivaroxaban to prevent the progression to severe COVID-19 [22].

Efforts to reduce COVID-19 mortality and morbidity are still ongoing. It established that patients

with COVID-19 pneumonia that show abnormal coagulation tests were associated with a fatal outcome [23]. Preliminary reports on using anticoagulants like therapeutic heparin in moderate COVID-19 to reduce COVID-19 mortality and morbidity suggest improved outcomes [24]. Experts' guidelines included prophylactic low-dose anticoagulants for adults admitted with moderate and severe COVID-19 but not the critically ill to reduce COVID-19 mortality [23,25]. Moreover, in a retrospective cohort study, up to half of venous thrombotic complications in hospitalized COVID-19 patients were diagnosed within the first 24 hours of admission [26]. Suggesting the importance of early use of anticoagulants for COVID-19 treatment. A prospective randomized open-label trial was conducted from 14 centres in Brazil to test the efficacy and safety of using Rivaroxaban [27].

Conclusion

Rivaroxaban 20 mg 1×1 as early treatment in moderate and severe COVID-19 cases can potentially protect from thrombotic events. Use with caution for reproductive-age women during menstruation is recommended.

Disclosure

None

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