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Research Article,

Assessing the Role of Coagulation Indicators and Chest CT Scans in Managing COVID-19 Inpatients at Omar Bongo Ondimba Army Training Hospital

Berthe Amélie Iroungou[1]; Adouni Mouyiwa Faousiath BOBO[2]; Jean Raymond Nzenze[2]; Laurette Guignali Mangouka[2]

[1]Unité Mixte de Recherche CIRMF-SSM, Libreville, Gabon
[2]Service de Médecine Interne, Hôpital d'Instruction des Armées Omar Bongo Ondimba, Libreville, Gabon
Email Address: **abertheamelie@gmail.com**

Abstract:

This retrospective descriptive study was conducted at the Omar Bongo Ondimba Army Training Hospital over a twelve-month period from January 1 to December 31, 2021. The study aimed to determine the impact of coagulation indicators, specifically D-Dimers and Prothrombin levels, on the management of COVID-19 inpatients and to evaluate the morphological aspects of COVID-19 on chest CT scans. A total of 179 inpatients were enrolled in the study, and data related to coagulation indicators were collected. Patients were classified according to clinical form, CT scan severity score, and different types of anticoagulant treatments.
The retrospective study found a sex ratio of 0.86 and the most represented age group was 50 to 59 years. D-Dimer levels were significantly higher in critical and moderate forms of COVID-19 (mean = 3812.8 ng/mL; median = 1683.5 ng/mL; IQR = 100 – 39743 ng/mL) compared to severe forms (mean = 1398.4 ng/mL; median = 699 ng/mL; IQR = 62 – 10000 ng/mL). Chest CT scans revealed pulmonary injury suggestive of COVID-19 pneumonia in 157 patients.
The study findings support the implementation of an anticoagulant protocol due to the co-occurrence of coagulation disorders and inflammatory signs with moderate and severe forms of COVID-19 and the presence of lung injury. Such a protocol can improve the morbidity and mortality of hospitalized patients.

Keywords: COVID-19, D-Dimers, Prothrombin Levels, Anticoagulant Treatment, Gabon

Introduction:

In December 2019, an outbreak of pneumonia cases with an unknown cause was identified in Wuhan, located in the Hubei province of China. The pathogen responsible for this outbreak was initially named 2019 novel coronavirus (2019-nCoV) and later identified as SARS-CoV-2 (1,2).
SARS-CoV-2 is primarily transmitted through respiratory droplets during close contact. The main clinical manifestation of COVID-19 is lung involvement, which can range from mild to severe. While some patients experience a favorable outcome, others may rapidly progress to a severe or critical form of COVID-19, characterized by acute respiratory distress syndrome, coagulation disorders, and multi-systemic organ failure. According to a 2021 study conducted in Gabon, 62.6% of patients with COVID-19 had mild or uncomplicated forms, while 33.7% had moderate forms, and 3.7% had severe forms (3,4).
Early identification of the severity of COVID-19 is crucial for timely clinical diagnosis and effective treatment. Coagulation indicators, such as D-Dimers (DD) and Prothrombin Levels (PR), are commonly used to sensitively reflect the coagulation status of COVID-19 patients. These indicators can aid in identifying severe forms of COVID-19 and assist clinicians in tailoring treatment plans to better manage the condition (5).
Between January 3, 2020, and April 1, 2022, Gabon experienced four waves of COVID-19. The severity of these waves ranged from moderate to critical forms, with respiratory tropism being the most commonly observed symptom. During this period, a total of 47,584 COVID-19 cases were

reported in Gabon, with 303 deaths being reported to the World Health Organization (WHO) (6,7)

The objective of this study was to evaluate the impact of D-Dimers (DD) levels, Prothrombin Levels (PR), and morphological aspects observed on chest CT scans in guiding the management of inpatients with COVID-19 at the Omar Bongo Ondimba Armed Forces Training Hospital (HIA-OBO). The study was conducted between September 2020 and December 2021.

Materials and Methods:

This retrospective descriptive study was conducted over a period of 12 months, from January 1 to December 31, 2021, at the Omar Bongo Ondimba Army Training Hospital. The study focused on adult patients diagnosed with COVID-19 and hospitalized for moderate, severe, or critical forms of the disease in the Department of Internal Medicine (COVID Unit) and Intensive Care Unit. Patient data was collected from medical records.

Clinical biochemistry was performed using COBAS C311 or C11 analyzers (Roche Diagnostics, Basel, Switzerland) to measure D-Dimers (DD), Prothrombin Levels (PR), and C-reactive protein (CRP) levels.

All chest CT scans were performed using a 64-slice CT scanner (Philips Brilliance CT 64; Philips). Pulmonary abnormalities were classified according to the extent and degree of involvement, with benign lesions involving less than 10%, moderate cases involving between 10% and 50%, and severe or critical cases involving more than 50% of the lung (8–10).

Statistical Analysis

Data collected from the medical records of patients diagnosed with COVID-19 at the Omar Bongo Ondimba Army Training Hospital were analyzed using Microsoft Excel 2016 and IBM-SPSS Statistics 22 software.

Ethical considerations

The study was approved by the National Scientific Committee of Gabon and the administration of the Omar Bongo Ondimba Army Training Hospital. All patients included in the study provided written informed consent, or in cases where patients were unable to provide written consent, they provided oral consent, which was documented. The study was conducted in accordance with ethical guidelines and regulations.

Results:

Sociodemographic characteristics

A total of 179 patients were included in the study, with a median age of 55 years. Of the study population, 53.6% were men, and 46.4% were women, resulting in a sex ratio of 0.86. The age group most represented was 50-59 years (25.7%), followed by the 60-69 years age group (24.6%). Patients over 70 years old were also well represented, accounting for 21.8% of the study population. The age groups of 40-49 years and 30-39 years accounted for 14% and 11.2%, respectively. Individuals under 30 years old were the least affected, accounting for only 2.8% of the study population.

Clinical features

Comorbidities were reported for 73.2% of the study population (131 patients). The most common comorbidities were high blood pressure (50.3%), type 2 diabetes (26.8%), and obesity (9.5%) (Table 1). The most frequently reported clinical signs were dyspnea, asthenia, and cough, with these symptoms being present in more than 40% of cases. The distribution of different functional signs is summarized in Figure 1.

The critical form of COVID-19 was the most dominant clinical form in the study population, accounting for 34.60% of cases. This was followed by moderate forms in 31.80% of cases and severe forms in 27.90% of cases.

Coagulation Factors and Inflammatory Parameters

D-Dimers were measured in 78 patients, which corresponds to 43.6% of the study population. The levels of D-Dimers were distributed according to different clinical forms, and the mean level was 2733 ng/mL, with a median of 1280 ng/mL (Table 2). Prothrombin Levels were measured in 71 patients, which accounts for 39.7% of the study population. Of these 71 patients, only 17 had a PR level below 70%. The median Prothrombin Level was 85% (Table 3). The CRP assay was performed in 104 patients, corresponding to 58.1% of the study population, and the median CRP level was 56 mg/L (Table 4).

Morphological aspects on chest CT scan

Chest CT scans were performed in 92.7% of patients, with 5% of scans being performed without the injection of iodinated contrast medium. The CT scans revealed lung lesions in the majority of cases (Figure 2). Images of chest

CT scans obtained upon admission to HIA OBO are shown in figures 3 to 6.

Criteria and Implementation of Anticoagulant Treatment

Anticoagulant treatment was started based on clinical, biological, and morphological criteria. Patients were required to have a clinical form of moderate, severe, or critical COVID-19, D-Dimers levels greater than 500ng/mL, increased levels of CRP above 6mg/l, a Prothrombin Level below 70%, and the presence of lung lesions on chest CT scans.

Out of the 179 patients included in the study, 170 patients (95%) received anticoagulant treatment. Of the nine patients hospitalized for critical illness, six died between 24 and 48 hours after admission.

The distribution of patients who received anticoagulant treatment according to clinical forms is shown in Figure 7. Among the patients who received anticoagulant treatment, 60 had D-Dimers levels greater than 500 ng/mL (Table 5). Prothrombin Levels were below 70% in 16 out of 170 patients who received anticoagulants (Table 6). CRP levels were greater than 40 mg/L in 57 out of 170 patients who received anticoagulants (Table 7). Among the 170 patients on anticoagulants, 157 had lesions on chest CT scans (Table 8).

Different anticoagulants were used at specific doses, with low molecular weight heparin (LMWH) such as Enoxaparin being administered at a prophylactic dose in 42.4% of cases and at a curative dose in 37.4% of cases. Calcium heparin, as an unfractionated heparin (UFH), was administered in 6.1% of patients, and oral anticoagulants were used in 0.6% of cases. Out of the 170 patients who received anticoagulant medicine, 120 had a positive outcome.

Figures et Tables

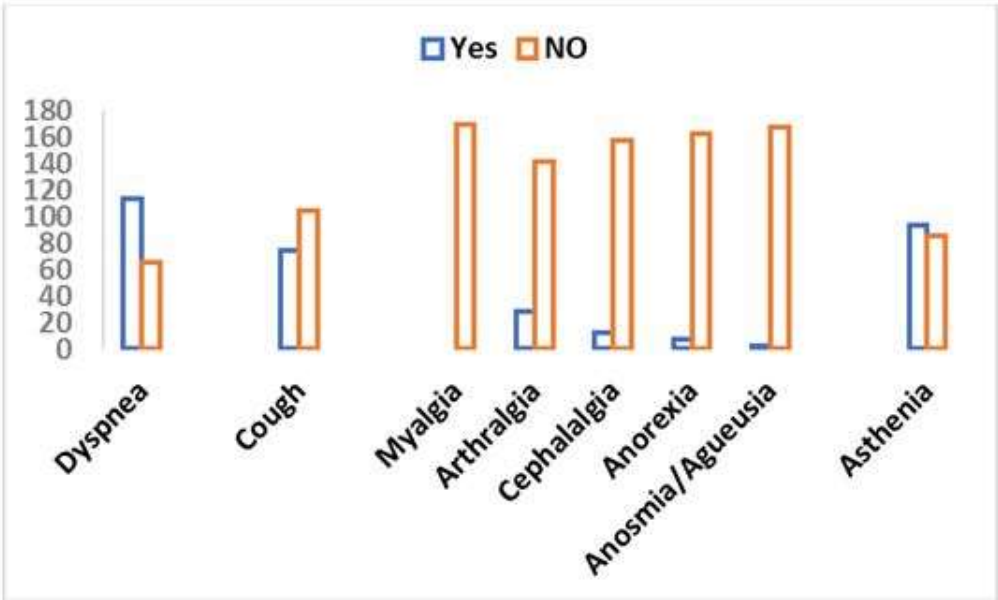

Figure 1: Distribution of Main Clinical Signs

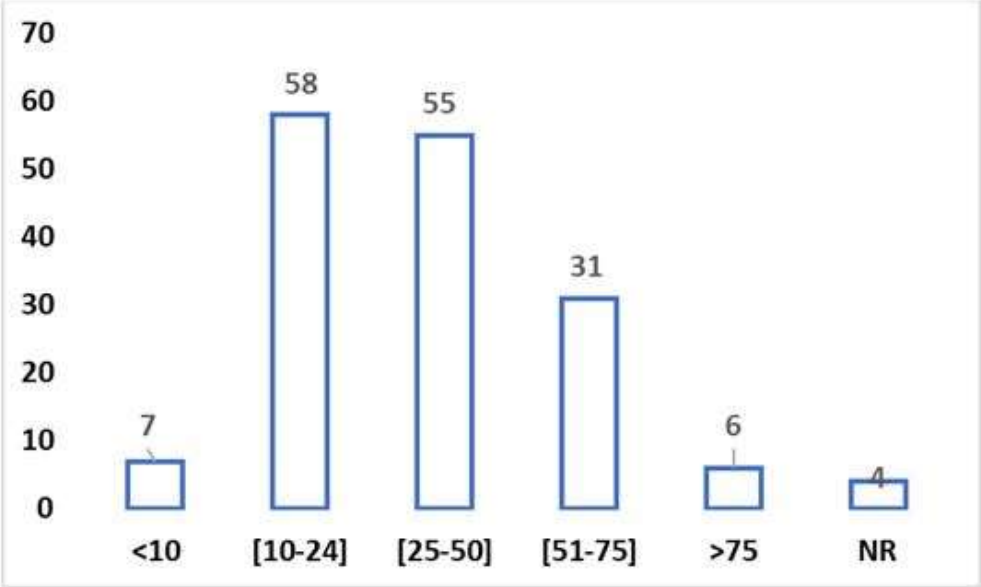

Figure 2: Patients with Lung Lesions on Chest CT Scans

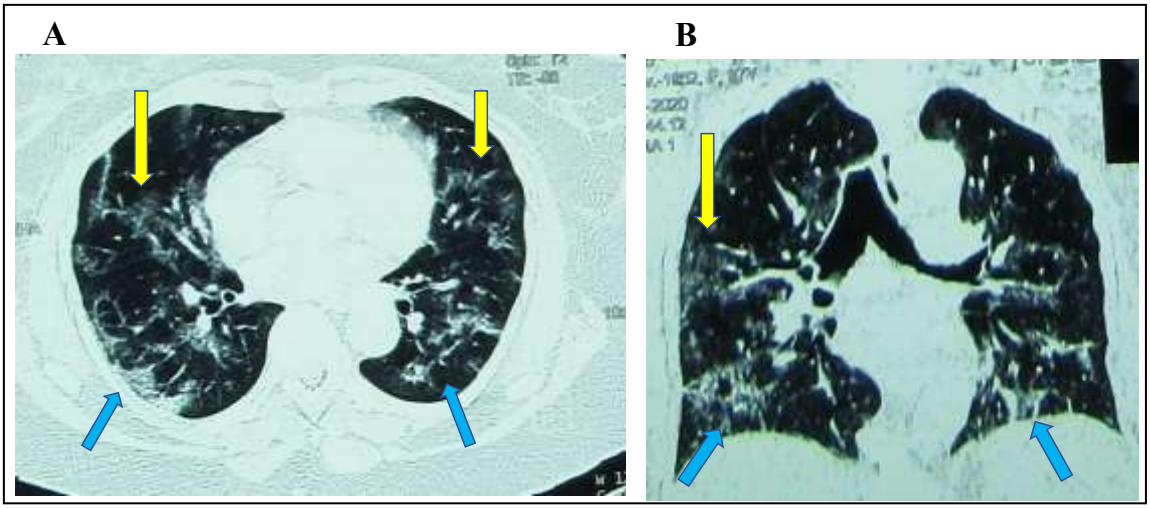

Figure 3: Representative chest CT scan images of moderate form of COVID-19 pneumonia with lung damage between 10-15% on chest CT scan without injection of iodinated contrast medium. (A) Axial and (B) sagittal view lung windows showing images of subpleural consolidation predominant in the right base (blue arrows) and diffuse ground glass (yellow arrows).

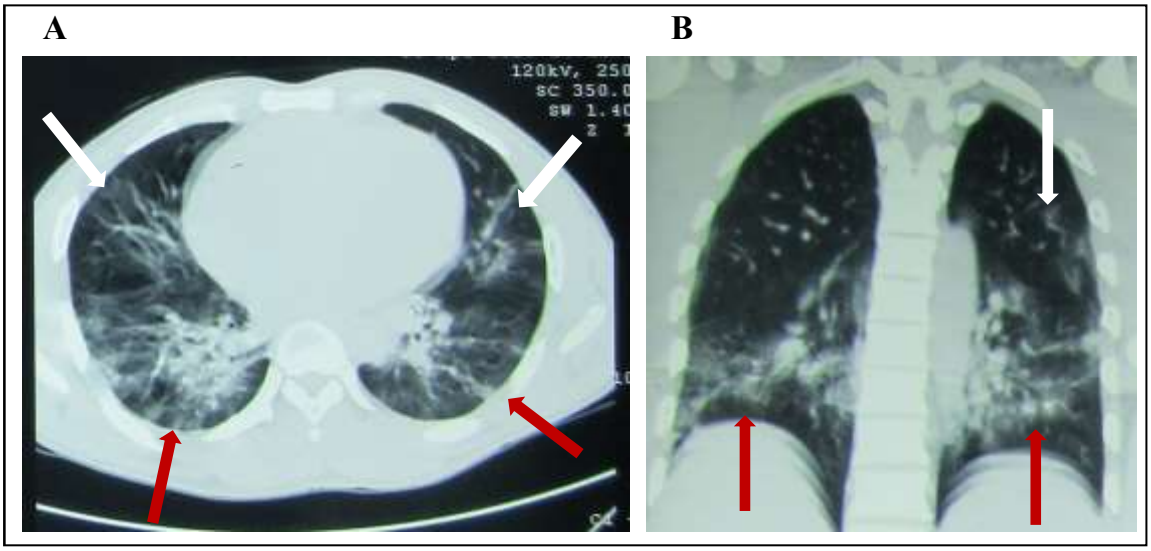

Figure 4: Chest CT scan showing a moderate form of COVID-19 pneumonia with lung damage between 20-25%. The axial (A) and sagittal (B) view lung windows displaying a predominant focus of subpleural consolidation mainly at the right lung base associated (red arrows) with bilateral ground glass (white arrows).

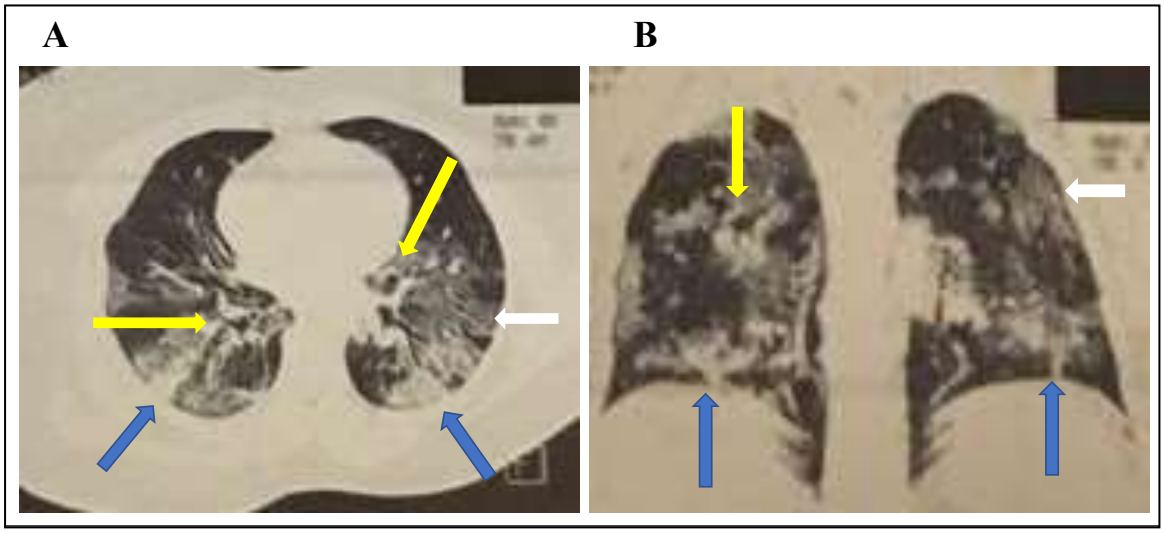

Figure 5: chest CT scan revealing a severe form of COVID-19 pneumonia with lung damage ranging between 60-70%. The images (A and B) show foci of parenchymal consolidation (blue arrows) associated with ground glass (white arrows), bilateral, predominantly at the lung bases and complicated with cylindrical bronchiectasis (yellow arrows).

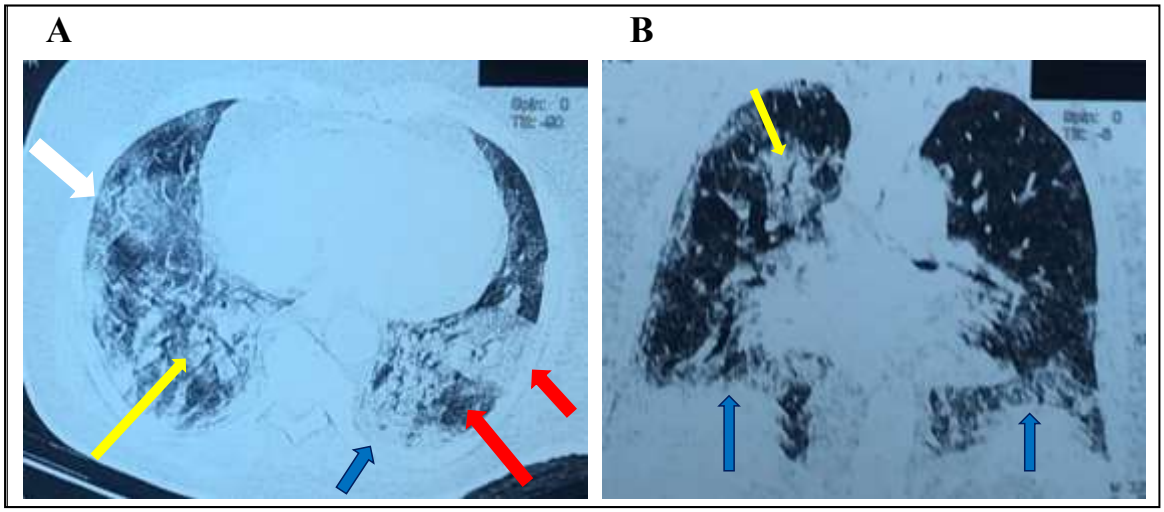

Figure 6: Chest CT scan with critical form of COVID-19 pneumonia between 70-80%. (A, B) showing foci of parenchymal condensation (bleu arrows) associated with ground glass (white arrow), bilateral, predominant at the level of the pulmonary bases and aspect of cylindrical bronchiectasis (yellow arrows) and images of "crazy paving" (red arrows).

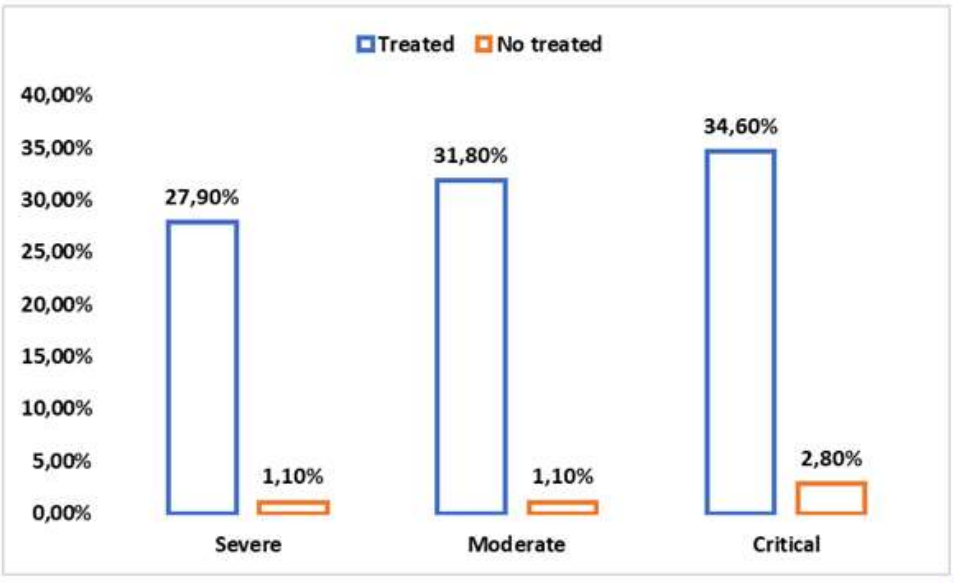

Figure 7: Clinical forms and anticoagulant treatment

Table 1. Comorbidities and COVID-19 inpatients.

Comorbidities	Effectif	Pourcentage
High blood pressure	90	50,3%
Type 2 diabetes	48	26,8%
Obesity	17	9,5%
Cerebral ischemic stroke	11	6,1%
Renal failure	10	5,6%
Cardiopathy	8	4,5%
Chronic lung disease	7	3,9%
HIV	5	2,8%
Surgery	4	2,2%
Cancer	3	1,7%
Sickle cell disease	2	1,1%
Psychiatric	2	1,1%
Dyslipidemia	2	1,1%
Cerebral vein thrombosis	1	0,6%
Endometriosis	1	0,6%
Hyperthyroidism	1	0,6%
Rheumatological	1	0,6%

Table 2. D-Dimers levels and clinical forms of COVID-19.

D-Dimères (ng/mL)	Clinical Forms of COVID-19		
	Critical	Moderate	Severe
< 500	3	10	4
[500 - 5000]	9	25	15
[5001 -10000]	7	2	2
> 10000	1	0	0
Unrealized	47	22	32
Total	**67**	**59**	**53**

Table 3. Prothrombin rate and clinical forms of COVID-19

Taux de prothrombine (%)	Clinical forms of COVID-19		
	Critical	Moderate	Severe
< 50	3	2	0
[50 - 69]	7	4	1
[70- 100]	14	26	14
Unrealized	43	27	38
Total	**67**	**59**	**53**

Table 4. CRP and clinical forms of COVID-19.

CRP (mg/L)	Clinical forms of COVID-19		
	Critical	Moderate	Severe
< 6	3	4	0
[6 - 40]	12	17	10
[41 - 100]	14	8	7
> 100	10	9	10
Unrealized	28	21	26
Total	**67**	**59**	**53**

Table 5. D-Dimers levels and anticoagulant treatment.

D-Dimères (ng/mL)	Anticoagulant treatment	
	No	
< 500	1	16
[500 - 5000]	0	49
[5001 -10000]	1	10
> 10000	0	1
Unrealized	7	94
Total	**9**	**170**

Table 6. Distribution of Anticoagulant Treatment according to Prothrombin levels.

Prothrombin rate (%)	Anticoagulant treatment	
	No	Yes
< 50	0	5
[50 - 69]	1	11
[70- 100]	2	52
Unrealized	6	102
Total	**9**	**170**

Table 7. CRP level and anticoagulant treatment

CRP (mg/L)	Anticoagulant treatment	
	No	Yes
< 6	0	7
[6 - 40]	2	37
[41 - 100]	0	29
> 100	1	28
Unrealized	6	69
Total	**9**	**170**

Table 8. Chest CT scan and anticoagulant treatment.

TDM (%)	Anticoagulant treatment	
	No	Yes
< 10	0	7
[10-24]	4	55
[25-50]	5	55
[51- 75]	0	34
> 75	0	6
No lesions	0	4
Unrealized	0	9
Total	**9**	**170**

Discussion:

The median age of COVID-19 inpatients in our study was 55 years (interquartile range: 50-59 years), which was similar to the median age of hospitalized patients in previous studies by *Wu et al.* (51 years (IQR: 43-60 years)) and *Zhou et al.* (56 years (IQR, 46-67 years)). Notably, *Iroungou et al.* reported a much younger median age of 35 years (interquartile range: 30-45 years), likely due to the relatively young population in Gabon (6,11,12).

These results suggest that older individuals may be more vulnerable to severe forms of COVID-19 due to age-related declines in adaptive and innate immunity (11,12).

We observed a predominance of males (53.6%) with a sex ratio of 0.86. This male predominance has also been reported by *Iroungou et al* and by

other studies carried out in some African countries such as Senegal and Burkina Faso but also by other authors around the world. This finding suggests that gender may be a factor influencing the susceptibility and/or severity of COVID-19 (6,13–17). However, there are studies that reported of a female predominance, highlighting other risk factors such as obesity (18,19).

We can explain our results by the fact that male sex hormones have been shown to promote the entry of SARS-CoV-2 by increasing the activity of Angiotensin 2 converting enzyme (ACE2) receptors, which are the entry point for the virus. Male sex hormones also exert immunosuppressive effects that can weaken the antibody response to infection, thus increasing the risk of severe disease (1,12,20).

Comorbidities, such as high blood pressure and diabetes, have been identified as risk factors for severity in patients with COVID-19 and are commonly reported in many studies worldwide, including our study. In our population, high blood pressure was the most common comorbidity, present in 50.3% of patients, followed by diabetes in 26.8%, and obesity in 9.5%. These findings are consistent with other studies conducted globally (21–24).

The predominance of high blood pressure disease and diabetes mellitus as comorbidities could be due to the increased expression of ACE2 receptors in cardiac epithelial, pancreatic β and vascular endothelial cells (11,12).

It could also be attributed to impaired innate immunity (first line of defense against SARS-CoV-2), chronic inflammation or high coagulation activity in patients with diabetes (4,25–27).

We observed significantly higher D-Dimers levels in severe and critical forms of COVID-19 (p=0.03) compared to moderate forms. The mean D-Dimers value in deceased patients was three times higher than in recovered patients. Other studies have also reported elevated D-Dimers levels in severe cases and deceased patients compared to moderate cases and survivors. *Chen et al.* observed an approximately seven-fold increase in normal D-Dimers values in severe COVID-19 cases compared to moderate cases (median 0.6 ng/mL, IQR: 0.3-1.3 ng/mL), while *Tang et al.* found D-Dimers levels 3 to 4 times higher in deceased patients compared to survivors (13,28–30).

Elevated D-Dimer levels have been shown to be a common finding in severe and critical forms of COVID-19, with significantly higher levels observed in deceased patients compared to survivors. This suggests a potential link between coagulopathy and the severity of the disease. Furthermore, D-Dimer levels have been shown to have prognostic value in patients with COVID-19 (12,31–34).

In our study, the PR was found to be between 40% and 100% in deceased patients. However, we did not observe any significant relationship ($p = 0.1$) between the variations in PR and clinical forms, such as severe and critical forms (mean = 80%; median = 83%) and moderate forms (mean = 82%; median = 68%). Furthermore, we did not find any significant relationship ($p = 0.1$) between the PR and favorable clinical outcomes. In a study by *Tang et al,* prothrombin rates were found to be modestly elevated in deceased patients. Nevertheless, according to *Merdji and al,* the measurement of PR does not seem to be sufficient for assessing the coagulopathy induced by COVID-19 (1,35–37). Based on these results, it can be inferred that prothrombin values alone may not be sufficient to determine the prognosis of patients with SARS-CoV-2 infection.

Chest CT scan without injection of contrast agent was an important tool in the orientation diagnosis in case of clinical suspicion of COVID-19 pneumonia. The predominance of ground glass could be related to the "cytokine storm" phenomenon, the deleterious mechanism of which promotes the progression of lesions within the pulmonary parenchyma (38–40).

The use of anticoagulant therapy in COVID-19 patients is a widely studied and recognized practice. Anticoagulant treatment was administered to 170 patients in our study based on a range of clinical, biological, and morphological criteria. Specifically, these patients met one or more of the following criteria: D-Dimers values > 500 ng/L (60 patients); PR < 70% (16 patients); CRP levels > 6 mg/L (94 patients); and parenchymal lesions on chest CT scan (157 patients). Notably, chest CT scan was the primary diagnostic tool used to initiate anticoagulant treatment in our series (41–43). The decision to start anticoagulant therapy was made in consideration of the significant risk of developing thromboembolic complications, such as pulmonary embolism and venous thromboembolic

disease, in hospitalized patients with COVID-19 (44–46).

The majority of anticoagulant treatments administered in our study (79.8%) consisted of LMWH, with UFH used in cases of significant renal impairment. Direct oral anticoagulants, such as Dabigatran, were used in only 0.6% of cases. While *International Society for Thrombosis and Haemostasis (ISTH)* guidelines recommends treatment with Enoxaparin 4000 IU/24 hours subcutaneously, some of the molecules suggested by the society were not available in our country. Therefore, the decision on which anticoagulant drugs to administer also took into account the tropical context and availability of such drugs in our pharmacies. Notably, our study found a lower mortality rate in patients who received anticoagulant treatment, and there was a statistically significant relationship (p=0.02) between anticoagulant treatment and clinical outcome (36,47–50).

Our study observed lower mortality in patients who received anticoagulant treatment, as well as a significant relationship between anticoagulant treatment and clinical outcomes (p=0.02). These findings are consistent with those of *Hani et al*, who observed lower D-Dimers values in hospitalized COVID-19 patients treated with anticoagulants compared to those who did not receive anticoagulant therapy (51,52). Furthermore, it was observed by *Tang et al.* that patients who received heparin for more than 7 days had a lower mortality rate compared to patients who did not receive this treatment (29).

These findings suggest that the risk of COVID-19 severity should be assessed in all patients admitted to the hospital for COVID-19 management, and the decision to administer anticoagulant therapy should be based on a variety of factors, such as clinical forms of COVID-19, increased D-Dimers levels, high CRP levels, and lung parenchymal involvement. Administering early and prolonged anticoagulant treatment as prophylactic and/or curative anticoagulation could limit the risk of hypercoagulability and hyper-inflammation linked to SARS-CoV-2.

Conclusion:

COVID-19 is a multi-faceted systemic disease that has a significant impact on coagulation. Indeed, blood hypercoagulability is common in patients hospitalized for moderate, severe, or critical forms of COVID-19. Thus, coagulation indicators, particularly D-Dimers values, should be systematically requested after a complete clinical exam to better assess the risk of severity of this disease. In the absence of biological tests, chest CT scan can help diagnose and indicate anticoagulant treatment. Therefore, the combination of all these biological and radiological tools would optimize follow-up and improve morbidity and mortality of patients in our region.

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