



Biological evaluation of coagulation problems in COVID-19 patients hospitalized at the centre hospitalier mère-enfant monkole, kinshasa, Democratic Republic of the Congo

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Abstract

Background: COVID-19 is a viral infection caused by SARS-CoV-2, which enters the body via the ACE2 receptor. This study aims to evaluate the coagulation disorders of COVID-19 patients admitted to Centre Hospitalier Mère-Enfant Monkole, Kinshasa.

Methods: This descriptive cross-sectional hospital-based study of patient files was conducted between July 2020 and June 2021 at CHME-Monkole in Kinshasa. The sample size was 130 patients using a random sampling technique after interviewing the respondents. For each respondent, biological and socio-demographic data were collected on a questionnaire. The primary analyses included the determination of PT, APTT, Plasma determination of D-dimers, and platelet count. A descriptive analysis was performed for socio-demographic characteristics, while Pearson correlation was used to determine the associations between socio-demographic characteristics and different biological parameters using SPSS 25.0. For ethical reasons, informed consent from patients was sought, and confidentiality was assured. The authorization was provided by the Ethical Committee of CHME-Monkole (Ethical code: KIN/CHME/04/2020).

Results: The findings showed D-dimer levels higher than 500 µg/L in 87.7% of respondents, prolonged APTT (>40 seconds) in 43.1% of respondents, PT (<70%) in 36.9% of respondents, and thrombocytopenia (platelets <150,000) in 26.2% of respondents. A positive correlation was observed between socio-demographic characteristics and D-dimer levels.

Conclusion: SARS-CoV-2 infection has a significant impact on coagulation. Thus, determining these biomarkers could predict the risk of disease severity or death in patients with COVID-19.

Introduction

Coronavirus 2019 (COVID-19) is a viral infection caused by the severe acute respiratory syndrome virus (SARS-CoV-2) (1, 2). SARS-CoV-2 is a single-stranded RNA virus that enters the body's cells via the angiotensin-converting enzyme 2 (ACE2) receptor (3, 4). This receptor is widely expressed in the body, particularly in the pulmonary alveoli and vascular endothelium (5, 6). WHO statistics on the coronavirus pandemic have revealed over 317 million infected cases and over 5 million deaths worldwide. Like all countries, the Democratic Republic of the Congo (DRC) was also affected by the COVID-19 pandemic, with 81,719 infected cases and 1225 deaths (7).

The disease is transmitted through close contact with infected persons. Most infected individuals initially present with respiratory failure, but some progress to more systemic disease and multi-organ dysfunction. The elderly and those with co-morbidities are at an increased risk of death from COVID-19 (8). The clinical manifestations reported during COVID-19 infection are vast. Among them, an inflammatory state can be very significant and lead to a cytokine storm and a prothrombotic state, resulting in thrombosis (9). This inflammation causes damage to the activation of the microvascular endothelium, which is probably at the origin of the manifestations of pulmonary or renal pathologies (9). Notably, 5% to 30% of hospitalized patients develop a clinically proven thrombotic event. Emerging evidence suggests that endothelial damage resulting from cell invasion by SARS-CoV-2 and subsequent dysregulation of the host response involving the inflammation and coagulation pathways play a crucial role in the progression of severe COVID-19 (10,11).

The most severely ill patients frequently observe coagulopathy and massive intravascular clot formation of the disseminated intravascular coagulation type. Therefore, coagulation and fibrinolysis tests help identify and monitor severe cases of COVID-19. Increased D-dimer levels, a relatively modest decrease in platelet count, and prolonged prothrombin time are typical findings in patients with COVID-19 and coagulopathy (12). This hemostatic imbalance is thought to contribute to organ failure, multisystem involvement, and death (13). In France, in a series of 107 consecutive COVID-19 cases admitted to an intensive care unit, 20% developed venous thromboembolism, despite standard pharmacological thromboprophylaxis and full-dose anticoagulation therapy. COVID-19 patients with acute respiratory syndrome were 6 times more likely to develop pulmonary embolism (13). However, the optimal way to prevent and treat the coagulopathies

that accompany COVID-19 would be to identify early markers of increased risk of thrombosis and the thrombotic complications that may ensue to help physicians prevent such complications (12, 13). The pathophysiology of microthrombosis is not yet well understood, and several hypotheses have been put forward. In the DRC, nearly 15% of COVID-19 patients are followed in different COVID-19 Treatment Centers. Of all these hospitalized patients, 41.4% were on oxygen in a severe and critical condition, all in Kinshasa, with a case fatality rate of 10% (14).

This study aimed to evaluate the coagulation disorders in COVID-19 patients admitted to Centre Hospitalier Mère et Enfant Monkole (CHME-Monkole), Kinshasa, DRC, from a biological perspective.

Methods

This descriptive cross-sectional hospital-based study on patient files was conducted between July 2020 and June 2021 at the Medical Biology Laboratory of CHME-Monkole in Mont-Ngafula municipality, Kinshasa, DRC.

As inclusion criteria, any person infected with the SARS-CoV-2 virus who was admitted to the hospital for therapeutic follow-up at CHME-Monkole and had samples sent to the Medical Biology Laboratory for analysis was included in the study. On the contrary, any person infected with SARS-CoV-2 who was not admitted and followed up at CHME was excluded from this study. The study population comprised patients with COVID-19 admitted to this health facility, and the sample size was 130 patients determined using a random sampling technique after conducting interviews based on a questionnaire.

For each respondent, epidemiological, clinical, biochemical, and hematological data and socio-demographic characteristics were collected using a questionnaire. The determination of Prothrombin time (PT), the Activated Partial Thromboplastin time (APTT), platelet count, and D-dimers were performed following the protocols of Mohammed et al. (15), Yorike et al. (16), Bashash et al. (17), Elkhalfifa (18), and Long et al. (19) with slight modifications. The normal ranges for PT were 10-15 seconds converted to a percentage (70-100%), for APTT were 30-40 seconds, for platelet count was 150,000-400,000/µL of blood, and for D-dimer was less than 500 µg/L (FEU). These values were used to

confirm abnormal cases and to find correlations between these biological parameters (PT, APTT, D-dimers, and platelet count) and socio-demographic characteristics.

Data entry was performed in Microsoft Excel and then exported to SPSS 25.0 for coding and analysis. A descriptive analysis (frequency and percentage) was conducted for socio-demographic characteristics, while Pearson correlation (Chi-square) was used to determine associations between socio-demographic characteristics and different biological parameters. Conversely, the correlation was applied to determine the relationship between socio-demographic characteristics and D-dimer levels. The significance level for statistical tests was $p < 0.05$, and the confidence interval was 95%.

For data collection in this study, informed consent was sought from patients after explaining the purpose of the research. The confidentiality and anonymity of the patients' data were assured. The study was authorized by the Ethical Committee of CHME-Monkole (Ethical code: KIN/CHME/04/2020).

Results

Most respondents are male (72%), and 28% are female. The distribution of respondents according to age group is described below. Figure 1 shows the distribution of respondents by gender.

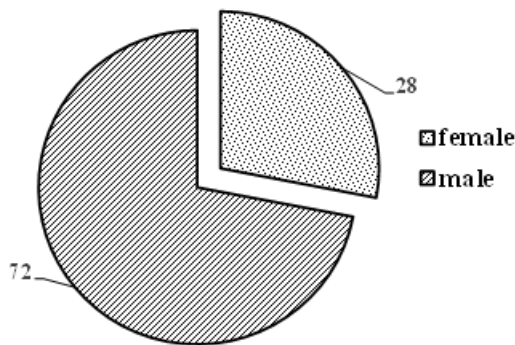


Figure 1: Gender distribution of respondents

It can be observed that 57.7% of respondents are in the 51-75 age group and 6.2% in the 0-25 age group. The relationship between normal and pathological values of different biological parameters is presented below.

Table 1. Distribution of respondents by age group

Age (years)	Frequency (n=130)	Percentage (%)
0-25	8	6.2
26-50	30	23.1
51-75	75	57.7
> 75	17	13.1
Total	130	100.0

Table 2. The ratio between normal and pathological values of the different biological parameters

Variables	Normal	Pathological
D-Dimers	16 (12.3)	114 (87.7)
PT	82 (63.1)	48 (36.9)
APTT	74 (56.9)	56 (43.9)
Platelets	96 (73.8)	34 (26.2)

PT=ProThrombin level, APTT=Activated Partial Thromboplastin Time

D-Dimers are more influential and/or pathological (87.7%) than the rest of the analyzed parameters.

The correlation between different biological parameters and socio-demographic characteristics is described below in Table 3.

It was observed that the 51-75 age group had a pathological D-dimer level (51.5%), a regular PT (40.8%), a normal APTT (36.2%), and a normal platelet count (41.5%). Among male respondents, the majority had a pathological D-dimer level (61.5%), while the remaining parameters were normal.

Table 3. Correlation between biological parameters and socio-demographic characteristics

Variables	Age (years)				Total
	0-25 (n=8)	26-50 (n=30)	51-75 (n=75)	> 75 (n=17)	
D-Dimers					
Normal	3 (2.3)	5 (3.8)	8 (6.2)	0 (0)	16 (12.3)
Pathological	5 (3.8)	25 (19.2)	67 (51.5)	17 (13.1)	114 (87.7)
PT					
Normal	2 (15)	18 (13.8)	53 (40.8)	9 (6.9)	82 (63.1)
Pathological	6 (4.6)	12 (9.2)	22 (16.9)	8 (6.2)	48 (36.9)
APTT					
Normal	5 (3.8)	19 (14.6)	47 (36.2)	3 (2.3)	74 (56.9)
Pathological	3 (2.3)	11 (8.5)	28 (21.5)	14 (10.8)	56 (43.1)
Platelets					
Normal	6 (4.6)	24 (18.5)	54 (41.5)	12 (9.2)	96 (73.8)
Pathological	2 (1.5)	6 (4.6)	21 (16.2)	5 (3.8)	34 (26.2)
Variables	Gender		Total		
	Male (n=93)	Female (n=37)			
D-Dimers					
Normal	13 (10)	3 (2.3)	16 (12.3)		
Pathological	80 (61.5)	34 (26.2)	114 (87.7)		
PT					
Normal	54 (41.5)	28 (21.5)	82 (63.1)		
Pathological	39 (30)	9 (6.9)	48 (36.9)		
APTT					
Normal	53 (40.8)	21 (16.2)	74 (56.9)		
Pathological	40 (30.8)	16 (12.3)	56 (43.1)		
Platelets					
Normal	65 (50)	31 (23.8)	96 (73.8)		
Pathological	28 (21.5)	6 (4.6)	34 (26.2)		

The symmetrical measurements between socio-demographic characteristics and D-dimers are presented in Table 4.

As the preliminary results are based on fewer than 1000 samples, it was observed that there is a positive relationship between age groups and D-dimer levels (n=130, r=0.233, and p=0.05). Similarly, a positive relationship exists between gender and D-dimer levels (n=130, r=0.081, and p=0.05).

Discussion

Regarding socio-demographic characteristics, it was observed that 72% of respondents were male. These findings are similar to those of Lumbulumbu (20), who reported the predominance of male respondents in Nord Kivu, which was also affected by COVID-19. In addition, it was observed that 57.7% of respondents were in the 51-75 age group, with a low representation of young people in the 0-25 age group (6.2%). This can be explained by the fact that more than 90% of deaths related to COVID-19 occur in the elderly due to various chronic pathologies and other medical histories. It is also due to the decrease in immune system efficiency when facing new pathogens that emerge or re-emerge compared to the youth with a very efficient immune system (21).

Different biomarkers of hemostasis were assessed in association with socio-demographic characteristics. The findings showed that the D-dimer assay presented very high values (>500 µg/L) in the 51-75 age group (51.6%) and among male respondents (61.5%). This study corroborates the findings of El Kettani (8), Tang et al. (10), Wu et al. (22), and Tang et al. (23).

Moreover, Tang et al. (23) reported that elevation of D-dimer levels (>500 µg/L) is frequent in this disease. The association between D-dimer elevation and disease severity has been confirmed, with a higher risk of mechanical ventilation or death (24). Tang et al. (10) noted that in deceased patients, there was a significant elevation of D-dimer and fibrin degradation products by 3.5 and 1.9 times, respectively, with a significant decrease in PT of 14%. Regarding the platelet count of respondents, it is usually normal or low (thrombocytopenia) on admission but may show dynamic changes during hospitalization. A low platelet

Table 4. Symmetrical measurements between socio-demographic characteristics and D-dimers

	Age				
	Values	Bias	Std.	CI (95%)	
Pearson's R	0.233	0.004	0.090	0.055	0.407
Spearman correlation	0.216	0.004	0.083	0.049	0.372
Kappa	0.007	0.000	0.025	-0.043	0.059
Total	130	0	0	130	130
	Gender				
	Values	Bias	Std.	CI (95%)	
Pearson's R	0.081	-0.005	0.078	-0.100	0.218
Spearman correlation	0.081	-0.005	0.078	-0.100	0.218
Kappa	0.036	-0.002	0.36	-0.0431	0.105
Total	130	0	0	130	130

count was identified as a poor prognostic factor in the elderly (25, 26). In this study, thrombocytopenia was noted in 26.2% of respondents. These findings are similar to those of Lamouasni (27), who also noted a low platelet count in patients affected by COVID-19. Thrombocytopenia is often considered an indicator of severity in sepsis. This also seems to be the case with SARS-CoV-2 infection, as thrombocytopenia was associated with a 5-fold higher risk of a severe form of the disease (28). SARS-CoV-2 inhibits hematopoiesis through CD13 receptors and can decrease the initial platelet formation, reduce many blood cells, and lead to thrombocytopenia (29).

It should be noted that PT and APTT are among the hemostasis parameters routinely measured and remain within normal values in most COVID-19 patients, including the most severe ones, both those hospitalized in intensive care and those presenting thrombotic events (30, 31). A decrease in PT may occur and suggest a diagnosis of disseminated intravascular coagulation (10). The APTT may indicate the presence of a lupus anticoagulant antibody (32), which is associated with a prothrombotic state.

In this study, the PT and APTT values were within the normal range for 63.1% and 56.9% of respondents, respectively. These findings are comparable to those of Helms et al. (33), who noted that 72% of PT and 67% of APTT were within normal limits in patients with COVID-19. Therefore, these standard coagulation parameters do not appear sufficient to assess COVID-19-induced coagulopathy; thus, exploring other blood parameters is necessary.

Conclusion

SARS-CoV-2 infection significantly impacts coagulation, with blood hypercoagulability being common in hospitalized individuals with COVID-19. These biological parameters could predict the risk of disease severity or death in people with COVID-19. These biomarkers will effectively help identify high-risk patients and allow for early and prolonged anticoagulation management. However, this study should be expanded by incorporating other important biomarkers such as Fibrinogen, Fibrin degradation products, etc., and utilizing other analytical techniques to enhance decision-making and ensure proper biological follow-up of COVID-19 patients.

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Ethical statement

An informed consent was sought from patients after explaining the purpose of the research. The confidentiality and anonymity of the patients' data were assured. The study was authorized by the Ethical Committee of CHME-Monkole (Ethical code: KIN/CHME/04/2020).

Conflicts of interest

The authors declare that there is no conflict of interest regarding the publication of this article.

Author contributions

MYM, GNB, NKN - Research concept and design, MYM, HN, EBB, YMM, JKM, CKK - Collection and/or assembly of data, MYM, JMV, GNB, NKN - Data analysis and interpretation, EBB, JNN, JJK - Writing the article, GNB, NKN - Critical revision of the article. All authors read and approved the final version of the article.

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