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Factors Associated with Death in Patients COVID-19 at the Epidemic Treatment Center of the Fann National University Hospital, Dakar

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Abstract: The aim of this study was to identify the factors associated with death in patients monitored for COVID-19 at the Epidemic Treatment Center (ETC) of the Fann National University Hospital (FNUH). This was a cross-sectional, retrospective, descriptive, and analytical study of patients hospitalized for COVID-19 during the period from 1 July 2021 to 31 March 2022. Patients aged 16 years or older hospitalized at the ETC of the NUH of Fann for COVID-19 confirmed by RT-PCR or rapid antigen test were included. Multivariate logistic regression was used to identify factors associated with death. During the study period, 248 patients were included. They had an average age of 61.7±15.2 years and were predominantly male 55.6%. High Blood Pressure (HBP) was the most common comorbidity (35.89%). 23.4% had been vaccinated against COVID-19. Dyspnea was the most frequent respiratory sign (77%), followed by cough (58.5%). Case fatality was 21%. In multivariate analysis, high D-dimer levels (ORa = 5.13; CI = [1.13-2.1]), the existence of a complication (ORa = 18.2; CI = [4.65-122]), and the absence of anticoagulant therapy (ORa = 0.01; CI = [0.00-0.14]) were the risk factors independently associated with death. Case fatality was 21%, the risk factors associated with death from COVID-19 being high D-dimer levels, the existence of a complication, and the absence of anticoagulant therapy.

Keywords: COVID-19, Associated Factors, Mortality, Dakar

Introduction

The SARS-COV2 infection known as COVID-19 broke out in China in December 2019 and was declared by the World Health Organisation (WHO) as a public health emergency of international concern on 30 January 2020 and a pandemic on 11 March 2020 (WHO, 2020). According to initial data, generally, 15% of people infected develop a severe form of the disease, with a case-fatality rate of around 3%, but it is higher in people of advanced age and those with co-morbidities, especially cardiovascular and metabolic (WHO, 2023a). As of 17 February 2023, 756,581,850 confirmed cases of COVID-19 had been reported, including 6,844,267 deaths worldwide (WHO, 2023b). Although Africa appears to be the continent least affected, 9,491,671 cases of COVID-19 had been confirmed by the same date, including 175,134 deaths (WHO, 2023b). In Senegal, well before the first case appeared on 02 March 2020, the Senegalese authorities reacted by putting in place a multisectoral national action plan for surveillance and response to the COVID-19 epidemic. This plan comprised several phases that could be adapted according to the epidemiological situation at the time and will be backed up by government measures. In addition, the majority of people affected by this new coronavirus suffer from mild forms of the disease and recover rapidly. Severely ill patients may progress rapidly to acute respiratory distress syndrome, multiple

organ failure, and even death (Huang *et al*., 2020). Despite the unprecedented national measures taken to combat the epidemic, as of 17 February 2023, there were 88916 confirmed cases in Senegal, including 1971 deaths, giving a case-fatality rate of 2.21% (Suivi du covid 19 au senegal en temps reel (n.d.)). Numerous studies published throughout the world have identified risk factors for a poor prognosis of COVID-19 (Zhou *et al.*, 2020; Alves de Oliveira *et al.*, 2023). For example, a cohort study conducted in Wuhan province in China showed that male sex, advanced age, and the presence of one or more comorbidities appear to play a significant prognostic role (Zhou *et al.*, 2020). A good understanding of the factors associated with death in patients with COVID-19 could therefore help strengthen prevention strategies to reduce mortality from this condition. The aim of this study was to identify the factors associated with death in patients monitored for COVID-19 at the epidemic treatment center of the Fann National University Hospital.

Materials and Methods

Study Design and Patient

The study was conducted at the ETC of the infectious diseases department of the Fann National University Hospital, which is a reference department for the management of infectious pathologies in Senegal and receives simple and severe forms of COVID-19. The study was a cross-sectional, retrospective, descriptive, and analytical study of patients hospitalized with COVID-19 during the period from 1 July 2021 to 31 March 2022. Patients aged 16 years or older hospitalized at the ETC of the NUH of Fann with COVID-19 confirmed by RT-PCR or rapid antigenic test during the period were included.

Data Collection

For this study, we opted for exhaustive sampling. Data were collected from patient's medical records and laboratory data using a Microsoft Excel Workbook (.xlsx) input mask. The following parameters were collected socio-demographic characteristics: Age, sex, geographical origin, vaccination status, co-morbidities (diabetes, HBP, obesity). Smoking habits. Clinical signs: Functional respiratory signs, general signs. Paraclinical signs: Haemogram, D-dimer level, creatinine level, transaminases, C-reactive protein level. Extent of scannographic lesions. Therapeutic and evolutionary aspects (death, cure, transfer).

Operational Definition of Variables

- The dependent variable of the study was death
- The independent variable we have:
  - Severe hyponatremia was defined as a natremia level <130 meq/l and hypernatraemia as a natremia level >145 meq/l
  - Hyperleukocytosis was defined as a white blood cell count greater than or equal to 12,000 cells/mm^3
  - Thrombocytopenia was defined as a platelet count of less than 150,000 cells/mm^3
  - Elevated C-reactive protein was defined as a level greater than or equal to 6 mg/L
  - D-dimer was considered to be elevated when its level was greater than 500 ng/mL
  - Creatinine was considered elevated when its level was greater than 13 mg/L
  - The extent of scannographic lesions was assessed according to the definition of the French Society of Radiology, with several stages including minimal (<10%), moderate (10-25%), significant (26-50%), severe (51-75%) and critical (>75%) involvement.

Statistical Analysis

The data were entered using Open Data Kit (ODK), then exported to Excel and analyzed using version 4.2.2 of R software. Qualitative variables were expressed as absolute and relative frequencies, and quantitative variables as average ± standard deviation or median (IQR) depending on the type of distribution. Factors associated with death were initially determined by bivariate analysis, using Fisher's exact test. Variables with $p<0.20$ were then entered into a model for multivariate analysis using logistic regression. At the end of this analysis, we had the adjusted Odds Ratios (ORa) for each explanatory variable framed by their IC95%. Values of $p<0.05$ were considered significant.

Results

Patient Characteristics

During the study period, we enrolled 248 patients. The average age of the patients was 61.7±15.2 years. Men predominated (55.6%), giving a sex ratio of 1.25. More than half of the patients (57.5%) lived in Dakar. High blood pressure was the most common comorbidity (35.89%), followed by diabetes (21.77%) and obesity (7.26%). Smoking accounted for 4.4% of patients. 58 patients (23.4%) had been vaccinated against COVID-19. Of the 58 patients vaccinated, 20 (34.5%) had received the Sinopharm vaccine. The average delay between the onset of COVID-19 and vaccination was 5.09±4.63 weeks [1-13 weeks]. Dyspnea was the most common clinical sign (77%), followed by physical asthenia (72.2%), cough (58.5%), and chest pain (24.6%). Fever was noted in 40% of patients. Of the 137 patients who had a blood count, 44% had hyperleukocytosis. Hepatic cytolysis was noted in 14.1% and creatinine levels were ≥13 mg/L in 20 patients. D-dimer levels were ≥500 ng/mL in 73.7% of patients and CRP levels were elevated in 92%. Of the patients who had chest CT scans, 72% had

ground-glass lesions. 88/160 (55%) of patients had severe to critical lesions. Anticoagulant therapy was instituted in 97.8% of patients, antibiotic therapy in 89.92%, and corticosteroid therapy in 93.59%. The average length of hospitalization was 7.49±6.04 days [0-38 days]. 52 patients died, giving a case fatality rate of 21%.

Factors Associated with Death

Bivariate Analysis

There were more deaths in patients aged over 60 years, as well as in male patients, although these were not risk factors for death. Smoking was associated with death (54.5% vs 20.9% p = 0.01). Dyspnea (p = 0.001) and the presence of complications (p<0.001) were factors associated with death (Table 1). Other factors associated with death in the bivariate analysis were hyperleukocytosis (p = 0.001), lymphopenia (p = 0.034), hypernatremia (p = 0.04), high D-dimer levels (p = 0.005) and severe to critical lung injury (p = 0.03) (Table 2). Deaths were higher in patients without anticoagulant treatment (54.5% vs. 20.9% p = 0.07).

Table 1: Bivariate analysis of epidemiological and clinical factors associated with death in patients with COVID-19 at the epidemic treatment center of the infectious diseases department of the Fann National University Hospital July 1, 2021, to March 31, 2022

	Death		
Variables	Yes N (%)	No N (%)	p-value
Sex			0,2
Female	19 (18.63)	83 (81,37)	
Male	33 (25.58)	96 (74.42)	
Age range (year)			0,31
<20	1(33.33)	2(66.66)	
[20–40[	1(5.26)	18(94.73)	
[40–60[	17(20.23)	67(79.76)	
≥60	33(26.40)	92(73.6)	
Covid vaccination			0,078
Yes	8 (13,79)	50 (86,20)	
No	44 (25.29)	130(74.71)	
High bool pressure			0,6
Yes	16 (20.0)	64 (80.0)	
No	36 (23.8)	115 (76.2)	
Obesity			0,5
Yes	5 (29.4)	12 (70.6)	
No	47 (22.0)	167 (78.0)	
Diabetes mellitus			0,20
Yes	14(29.2)	34 (70.8)	
No	38 (20.8)	145 (79.2)	
Chronic Kidney disease			0,3
Yes	7 (35.00)	13 (65.00%)	
No	45 (21.33)	166 (78.67)	
Smokers			0,018
Yes	6 (54.5)	5 (45.5)	
No	46 (20.9)	174 (79.1)	
Thoraciq pain			0,48
Yes	10 (18.2)	45 (81.8)	
No	42 (23.9)	134 (76.1)	
Dyspnae			0,001
Yes	50 (27.9)	129 (72.1)	
No	2 (3.8)	50 (96.2)	
Complications			<0,001
Yes	49(50.52)	48 (49.48)	
No	3 (2.24)	131 (97.76)	

Table 2: Bivariate analysis of biological and scannographic factors associated with death in patients with COVID-19 at the epidemic treatment center of the infectious diseases department of the Fann National University Hospital July 1, 2021, to March 31, 2022

	Death		
Variables	Yes n (%)	No n (%)	p-value
White blood cell N = 1 37			
Hyperleukocytosis	22 (36.0)	39 (63.93)	0,001
Leukopenia	2 (33.3)	4 (66.7)	
Normal	9 (12.9)	61 (87.1)	
Lymphocyte count N = 103			0,034
Lymphocytosis	1 (33.3)	2 (66.7)	
Lymphopenia	13 (43.3)	17 (56.7)	
Normal	13 (18.6)	57 (81.4)	
Platelet N = 130			
Thrombocytosis	4 (19.0)	17 (81.0)	0,804
Thrombocytopenia	5 (27.8)	13 (72.2)	
Normal	20 (22.0)	71 (78.0)	
D-dimer (mg/L) N = 107			0,005
Elevated	24 (30.0)	56 (70.0)	
Normal	0	27 (100)	
C-reactive protein (mg/L)N = 141			0,15
Elevated	31 (23.7)	100 (76.3)	
Normal	0 (0.00)	10 (100)	
Natremia N = 137			0,04
Hypernatremia	3 (60.0)	2 (40.0)	
Hyponatremia	6 (33.3)	12 (66.7)	
Normal	22 (19.3)	92 (80.7)	
Kaliemia N = 137			0,128
Hyperkaliemia	6 (46.2)	7 (53.8)	
Hypokaliemia	1 (14.3)	6 (85.7)	
Normal	24 (20.5)	93 (79.5)	
Extent of CT lesions N = 160			0,03
Mild	2 (8.7)	21 (91.3)	
Moderate	7 (18.4)	31 (81.6)	
Important	1 (9.1)	10 (90.9)	
Severe	19 (38.0)	31 (62.0)	
Critical	11 (28.9)	27 (71.1)	

Multivariate Analysis

High D-dimer levels, absence of anticoagulant treatment, and the occurrence of complications were the risk factors independently associated with death (Fig. 1). High D-dimer levels multiplied the probability of death by a factor of 5.13 (ORa = 5.13; CI= [1.13-32.1]). The existence of a complication multiplied the probability of death by 18.2 (ORa = 18.2; CI = [4.65-122]). The absence of anticoagulant treatment multiplied the risk of death by 99% (ORa = 0.01 [0.00-0.14]).

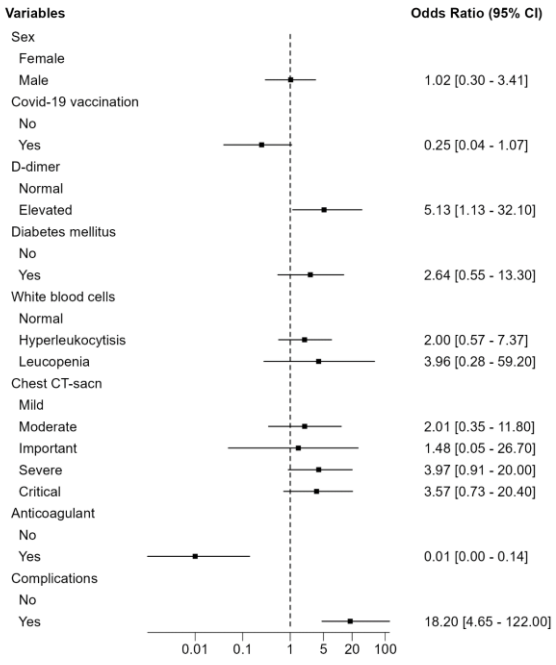

Fig. 1: The forest plot of Multivariate analysis: Factors associated with death in patients with COVID-19 at the epidemic treatment center of the infectious diseases department of the Fann National University Hospital July 1, 2021, to March 31, 2022

Discussion

A great deal of effort has been made in the fight against COVID-19, which has nevertheless caused many deaths throughout the world. Knowledge of the factors associated with death in these patients could help improve prevention strategies. In our series, a fatality rate of 21% was noted. These results corroborate other studies conducted in Burkina Faso (Ouédraogo *et al.*, 2021), Mali (Sy *et al.*, 2023), and Guinea (Donamou *et al.*, 2021), which reported an overall case-fatality rate of 25% or less. This contrasts with studies conducted in China (29.2%) (Terre *et al.*, 2019), the United States (39%) (Cummings *et al*., 2020), and Brazil (47.2%) (Baqui *et al.*, 2020), where a higher rate was found. Nevertheless, the case fatality rate remained high because the Fann epidemic treatment center received most of the severe cases during the pandemic. This difference could be explained in part by the fact that the African population is less young than in the countries of the North.

Advanced age has been described as a risk factor for severe disease in COVID-19. Studies in the general population support the view that age is an important risk factor for clinical severity and death, due to the senescence of the immune system (Zhou *et al*., 2020; Semenzato *et al*., 2020; Jaspard *et al*., 2021; Wastiaux *et al*., 2020). Indeed, in a multicentre study conducted in Guinea, there were more deaths in COVID-19 patients aged over 60 OR: 24.93 and P: 0.000 (95% CI: 12.30-50.53) (Kpamy *et al*., 2020). In a study conducted in Mexico, age over 40 years was the leading epidemiological risk factor for death in COVID-19 patients (HR = 4.21; 95% CI [3.59-4.93) (Chiquete *et al*., 2022). The same trend has been reported in China (HR = 12.58; 95% CI [6.78-23.33]) (Zhang *et al*., 2022). However, in our study, although the number of deaths was higher in patients aged 60 and over, age did not appear to be a risk factor for death. Numerous studies in the literature have analyzed the association between gender and death in patients with COVID-19, with controversial results. In our predominantly male study, there was no association between gender and death (p = 0.2). This result is similar to that of a study conducted by Wastiaux *et al*. (2020). However, a significant difference was reported in two studies in France (Semenzato *et al*., 2020) and West Africa (Jaspard *et al*., 2021). This may be explained by the fact that there are biological differences between men and women, particularly in terms of the immune system and hormones.

In addition, in our series, the independent factors associated with death were an elevated D-dimer level, the occurrence of complications, and the absence of anticoagulant treatment in the patients. D-dimers greater than 500 ng/mL were associated with fatal outcomes in COVID-19 (ORa = 5.13 [1.13-32.1]). These data are in line with the literature (Zhou *et al*., 2020; Tang *et al*., 2020). This could be explained by the fact that high D-dimer levels reflect vascular microthrombosis in the context of coagulopathy associated with COVID-19 and are associated with the severity of the disease and the risk of admission to intensive care and death (Tazi Mezalek, 2021).

The occurrence of complications was independently associated with death (ORa = 18.2 [4.65-122]) in our cohort. This is in line with other studies (178 Guan *et al*., 2020; Zhou *et al*., 2020; Docherty *et al*., 2020) in the UK where the authors generally suggest that the presence of complications is an important predictor of death from COVID-19. The occurrence of complications often indicates more severe damage to the organism, impacting vital functions. This is often the reason for management with close monitoring and advanced medical interventions. Despite these measures, some patients may not respond to available treatments, increasing the risk of death. In our study, comorbidities were not associated with death. However, it is important to note that pre-existing co-morbidities may also play a role in the occurrence of complications and the risk of death (Ouédraogo *et al*., 2021). Certain underlying medical pathologies, such as cardiovascular diseases, diabetes, and obesity, may increase a person's vulnerability to developing serious complications of COVID-19.

Concomitantly, the absence of anticoagulant treatment multiplied the risk of death by 99% (ORa = 0.01 [0.00-0.14]). Indeed, the studies by Paranjpe *et al*. (2020);

Lopes *et al*. (2021) suggest that anticoagulation, either in prophylactic or therapeutic doses, may play a protective role against COVID-19 related deaths, particularly in patients with hypercoagulability-or-signs-of-coagulation-dysfunction. This is because anticoagulation can help prevent the formation of excessive blood clots and reduce thromboembolic complications associated with COVID-19, such as pulmonary embolisms or strokes.

Some authors have reported that COVID-19 vaccination has been described as an effective means of preventing severe disease, hospitalization, and death associated with COVID-19 (Levine-Tiefenbrun *et al*., 2021, Dagan *et al*., 2021, Thompson *et al*., 2021). Levine-Tiefenbrun *et al*. (2021) pointed out that vaccines against COVID-19 disease could reduce the viral load during breakthrough infections and thus further suppress transmission. However, vaccination against COVID-19 is neither a risk factor for death nor a protective factor in our cohort. This may be explained by the fact that only 23.4% of our study population had been vaccinated against COVID-19. This may be due to reluctance to vaccinate against COVID-19, given that the study period corresponded to the 3rd and 4th waves in Senegal.

Strengths and Limitations of the Study

This first study in a reference Centre provides an overview of the factors associated with death during the management of COVID-19 during this pandemic in our context. The retrospective nature of the study means that some of the missing data, particularly concerning patients' comorbidities, have hampered the exploration of the association between comorbidities and death. This study opens up the prospect of further work on longitudinal studies.

Conclusion

This study conducted at the Fann Epidemic Treatment Center in Dakar found that more than half of the patients had severe to critical forms of the disease. The case fatality rate was 21% and the risk factors associated with death from COVID were high D-dimer levels, the existence of a complication, and the absence of anticoagulant therapy. Knowledge of these factors is essential if we are to assess the risks more accurately, strengthen management strategies, and implement appropriate measures.

We recommend early detection of patients at risk of complications, D-dimer testing, and the use of anticoagulants in patients with severe to critical forms of the disease.

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Author's Contributions

Viviane Marie Pierre Cisse: Coordinated the research, designed the research plan, coordinated the data collection, and wrote the manuscript.

Khardiata Diallo Mbaye: Contributed to the data collection and data entry process.

Ndèye Maguette Fall: Conducted the data collection and writing of the manuscript.

Khardiatou Barro: Contributed to the data collection, analyzed data, and wrote the manuscript.

Bruce Wembula: Contributed to analyzing data.

Assane Diouf, Papa Latyr Junior Diouf, Alassane Sarr, Daouda Thioub, Ndèye Aïssatou Lakhe, Papa Samba Ba, Daye Ka and Louise Fortes: Contributed to the data collection.

Amadou Alpha Sall: Contributed to biological analysis.

Moussa Seydi: Coordinated the research.

Ethics

This article is original and contains unpublished material. The corresponding author confirms that all of the other authors have read and approved the manuscript and that no ethical issues are involved.

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