Scientific Research Publishing

Advances in Infectious Diseases, 2023, 13, 117-131
https://www.scirp.org/journal/aid
ISSN Online: 2164-2656
ISSN Print: 2164-2648

Risk Factors for COVID-19 Related Death during the First Three Waves of the Pandemic in an Epidemic Treatment Center at Dakar, Senegal

Moustapha Diop[1*], Papa Samba Ba[1], Viviane Marie Pierre Cisse[2], Ndèye Aissatou Lakhe[2], Betty Fall[1], Moustapha Lo[1,3], Ndong Essomba[4], Bruce Wembulua[2], Fatimata Wone[5], Becaye Fall[6], Khardiata Diallo-Mbaye[2], Daye Ka[2], Louise Fortes[5], Ousmane Faye[7], Ndongo Dia[7], Khalifa Ababacar Wade[8], Abdou Rajack Ndiaye[9], Amadou Alpha Sall[7], Moussa Seydi[2], Mame Thierno Dieng[9]

[1]Epidemic Treatment Center, Dakar Principal Hospital, Dakar, Senegal
[2]Infectious and Tropical Diseases Department, FANN Teaching Hospital, Dakar, Senegal
[3]Psychiatry Department, Dakar Principal Hospital, Dakar, Senegal
[4]Internal Medicine Department, Deido District Hospital, Douala, Cameroon
[5]Dalal Jamm Hospital, Dakar, Senegal
[6]Federation of Laboratories, Dakar Principal Hospital, Dakar, Senegal
[7]Pasteur Institute of Dakar, Dakar, Senegal
[8]Anesthesia-Resuscitation Department, Dakar Principal Hospital, Dakar, Senegal
[9]Dakar Principal Hospital, Dakar, Senegal
Email: *mouztaphandm@gmail.com

How to cite this paper: Diop, M., Ba, P.S., Cisse, V.M.P., Lakhe, N.A., Fall, B., Lo, M., Essomba, N., Wembulua, B., Wone, F., Fall, B., Diallo-Mbaye, K., Ka, D., Fortes, L., Faye, O., Dia, N., Wade, K.A., Ndiaye, A.R., Sall, A.A., Seydi, M. and Dieng, M.T. (2023) Risk Factors for COVID-19 Related Death during the First Three Waves of the Pandemic in an Epidemic Treatment Center at Dakar, Senegal. *Advances in Infectious Diseases*, **13**, 117-131.
https://doi.org/10.4236/aid.2023.132013

Received: February 24, 2023
Accepted: April 25, 2023
Published: April 28, 2023

Abstract

Introduction-Objective: COVID-19 is a highly transmissible but often mild viral infection. However, some patients can present severe COVID-19 and subsequently die. The aim of the present study was to assess the risk factors for COVID-19 related death during the first three waves of the disease at the Epidemic Treatment Center (ETC) of Dakar Principal Hospital (DPH). **Method:** We conducted a descriptive and analytical perspective survival study from April 4, 2020 to September 25, 2021, including adult patients with COVID-19, hospitalized at the ETC of DPH. Log Rank test and multivariate Cox model were performed to identify risk factors for death. **Results:** We included 556 COVID-19 patients with mean age of 57 ± 17 years and a male-to-female ratio of 1.26. The number of deaths during one month of follow-up was 41, representing a cumulative risk of 7.4%. The log Rank test showed that being from the third wave ($p = 0.0056$), advanced age ($p = 0.00098$), presence of at least one comorbidity ($p = 0.034$), High blood pressure ($p = 0.024$), d-dimer level ≥ 1000 IU/L ($p < 0.001$) and CRP level ≥ 12 mg/L ($p = 0.014$) appeared to be risk factors for death. In multivariate Cox

regression, the third wave of the pandemic (HR = 2.25; 95% CI [1.08 - 4.68], p = 0.03) and advanced age (HR = 2.68; 95% CI [1.23 - 5.85], p = 0.013) were risk factors for death. **Conclusion:** Our study showed that elderly and third-wave of COVID-19 patients were more at risk to die. Knowledge of risk factors for COVID-19 related death could improve the prognosis of these patients.

Keywords

COVID-19, Waves, Death, Risk Factors, Dakar

1. Introduction

COVID-19 is a highly contagious acute viral disease due to Sars-Cov2 which was discovered in late 2019 [1]. Due to its rapid spread, WHO declared it a global public health emergency of international concern on January 30, 2022, before considering it a pandemic on March 11, 2020 [2] [3]. It remains a worldwide public health threat despite its downward trend during anti-COVID-19 vaccination period. As of February 21, 2023, the cumulative number of confirmed cases worldwide since the start of the pandemic was 757,264,511 with 6,850,594 deaths. In Senegal, more than 88,850 confirmed cases and 1968 deaths were recorded at the same period [4]. The clinical presentation of Sars-Cov2 infection remains benign in most cases. It is often limited to asymptomatic or mild general and/or respiratory signs [5]. However, there are severe and critical COVID-19 that can lead to death from hypoxemic pneumonia or thromboembolic events, when early and adequate management is not undergone [7]. According to many authors, some factors such as advanced age, male gender or the presence of comorbidities are known to be associated with these severe COVID-19 [7] [8] [9]. Although the death rate of COVID-19 is much higher in developed countries, this pandemic causes a high number of deaths in Africa and Senegal. However, in most of African studies, prognostic factors for death in patients with COVID-19 have been evaluated exclusively during the first wave of the pandemic [10] [11] [12]. Additionally, in Senegal as in many other African countries, intra-hospital management of COVID-19 was more effective during the first three waves. Outpatient follow-up was preferred beyond those waves, due to the predominance of mild clinical presentations of the disease. This is the reason why we carried out this present study during the first three waves of the pandemic with the aim of evaluating the risk factors for COVID-19 related death in the Epidemic Treatment Center (ETC) of Dakar Principal Hospital (DPH).

2. Materials and Methods

2.1. Period and Study Design

We conducted a single centre prospective survival study covering the period

from April 4, 2020 to September 25, 2021.

2.2. Study Population

Our Study population included patients admitted in the Epidemic Treatment Centre of Dakar Principal Hospital during the first three waves of the COVID-19 pandemic. Among them, we enrolled patients who were at least 16 years of age with confirmed SarsCov2 infection by RT-PCR or rapid antigen test of nasopharyngeal or oropharyngeal samples. Patients with suspected COVID-19 symptoms were tested. Those unwilling to participate in the study and those with less than 24 hours of hospitalization in the ETC were not eligible for enrolment.

2.3. Data Collection

Data were collected through individual interviews with patients and medical records. An exhaustive sampling method was adopted. Tested questionnaire designed by investigators of the study has been used to collect information needed and a previously trained investigator was in charge to collect data. Information such as sociodemographic characteristics (age, sex, marital and smoking statutes), comorbidities (including diabetes, high blood pressure, obesity, pre-existing heart disease, asthma, chronic obstructive pulmonary disease (COPD), HIV infection, chronic kidney disease, or other comorbidities), Clinical features (the delay in diagnosis of the disease defined as the time period from the onset of symptoms to COVID-19 confirmations, vital signs, symptoms), laboratory parameters (C-reactive protein and d-dimer levels), Treatment received, number of hospital days and outcomes (death, transferred or cured) were collected.

2.4. Data Management and Statistical Analysis

Data were recorded in Epi info software (version 7.2.2.6), exported to Excel and were subsequently analysed using R software (version 4.0.3) after checking and cleaning the database. Qualitative variables were expressed using absolute and relative frequencies. Continuous variables were reported as means (m) with standard deviations (sd) if normally distributed; otherwise medians with interquartile range (IQR) were used. To evaluate the risk factors for COVID-19 related death, we considered the time origin as the day of hospitalization for each patient. A follow-up time of one month was defined for each of them regardless of the date of admission. The event of interest was the "death" variable (1 = occurrence of death; 0 = absence of death). Dependent variables included age, sex, wave of COVID-19, marital status, comorbidities, delay of diagnosis, d-dimers and CRP rates. Kaplan Meier method was used to determine the cumulative death rate over time of follow-up. Log Rank test was performed to compare the instantaneous death rates between two or several groups of individuals. To adjust for potential confounding factors, we performed a multivariate Cox proportional hazard regression. All candidate explanatory variables with a p-value < 0.25 in the Log Rank test have been included in the multivariate model to calcu-

late their adjusted hazard ratios (aHR) with 95% confounding intervals (95%CI). Variables with more than 10% of missing values were removed from the dataset as well as individuals with missing values on the remaining variables. Schoenfeld adequacy test and interaction checking between independent variables were performed to validate the multivariate Cox model. For all the analyses, statistical significance was set at p-value = 0.05.

2.5. Ethical Considerations

Our study design was observational and did not require any examinations or other interventions involving physical or psychological damage to the participants. Free and informed consent was accorded by the patients before being eligible to be enrolled. To preserve confidentiality and anonymity, initials of first and last name were used in the questionnaire. Information was recorded in a secure database with an identification code assigned to each patient. Therapeutic management based on the national COVID-19 guideline was provided.

3. Results

3.1. Epidemiological Characteristics of Patients

During the study period, 560 patients with COVID-19 were admitted to the ETC of the DPH. Of those hospitalized, one had less than 24 hours of stay length and three were under the age of 16 (2 newborns and a 9-year-old child). This reduced our study population to 556 patients. Most of them (43%) were from the first wave of the pandemic which was longer with duration of 7 months. The second and third waves lasted 6 months and 5 months, respectively. The rate of patients' admissions over time, represented in Figure 1, was similar to the national epidemiological curve of the pandemic with hospitalization peaks in August 2020 for the first wave, January 2021 and July 2021 for the second and third

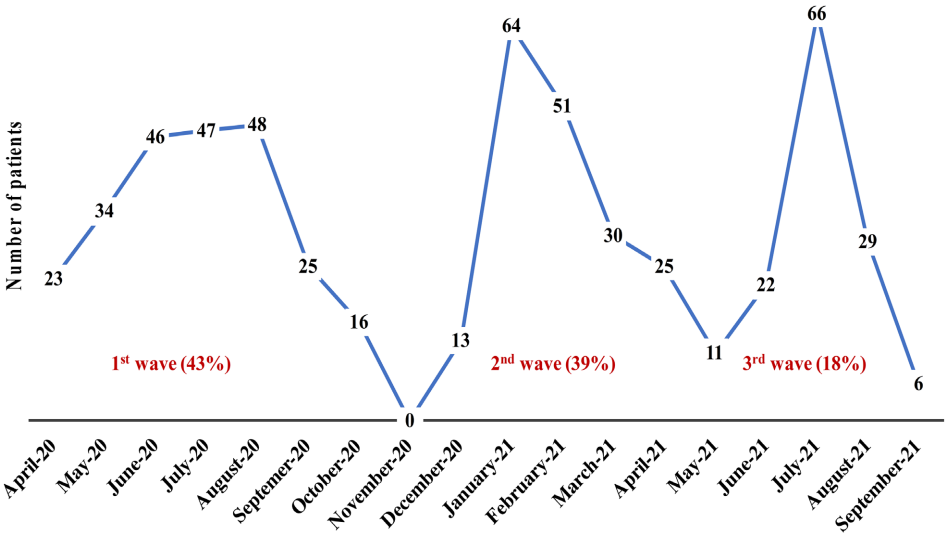

Figure 1. Distribution of patients with COVID-19 according to months of admission to the ETC of DPH (April 2020-September 2021): N = 556.

wave, respectively.

The mean age of the study population was 57 years ± 17 years and the most represented age group during all three waves was that of more than 60 years with a global proportion of 48%. Patients of the second and third wave were slightly older with respective mean ages of 60 ± 15 years and 58 years ± 16 years versus 53 years ± 18 years for those of the first wave. There were persistently more men than women during the whole three waves with a global sex ratio of 1.26 (310/246). More than half of patients had at least one comorbidity and the most represented remained high blood pressure and diabetes with global proportions of 31% and 26%, respectively (Table 1).

Table 1. Epidemiological characteristics of patients with COVID-19 at the ETC of DPH (April 2020-September 2021).

Epidemiological characteristics	Global population N = 556 *	1st wave N = 239 *	2nd wave N = 216 *	3rd wave N = 101 *
Age (years)	57 ± 17	53 ± 18	60 ± 15	58 ± 16
Age groups (years)				
[18 - 40[	106 (19%)	71 (30%)	19 (8.8%)	16 (16%)
[40 - 60[	182 (33%)	67 (28%)	79 (37%)	36 (36%)
≥ 60	268 (48%)	101 (42%)	118 (55%)	49 (49%)
Sex				
Female	246 (44%)	101 (42%)	96 (44%)	49 (49%)
Male	310 (56%)	138 (58%)	120 (56%)	52 (51%)
Marital status				
Singles	47 (11%)	38 (16%)	7 (4.2%)	2 (8.3%)
Divorced	25 (5.9%)	9 (3.8%)	15 (9%)	1 (4.2%)
Married	325 (76%)	178 (75%)	128 (77%)	19 (79%)
Widowed	30 (7%)	12 (5.1%)	16 (9.6%)	2 (8.3%)
Marital regime				
Monogamy	86 (66%)	55 (73%)	21 (50%)	10 (71%)
Polygamy	45 (34%)	20 (27%)	21 (50%)	4 (29%)
Smoker	35 (6.3%)	18 (7.5%)	14 (6.5%)	3 (3.0%)
Comorbidities	318 (57%)	131 (55%)	130 (60%)	57 (56%)
High blood pressure	171 (31%)	68 (28%)	73 (34%)	30 (30%)
Diabetes	147 (26%)	61 (26%)	56 (26%)	30 (30%)
Obesity	14 (2.5%)	5 (2.1%)	4 (1.9%)	5 (5.0%)
Asthma	39 (7%)	17 (7.1%)	20 (9.3%)	2 (2.0%)
COPD	8 (1.4%)	3 (1.3%)	4 (1.9%)	1 (1.0%)
heart disease	24 (4.3%)	9 (3.8%)	11 (5.1%)	4 (4.0%)
Chronic Kidney disease	8 (1.4%)	2 (0.8%)	5 (2.3%)	1 (1.0%)

*Mean (m) ± standard deviation (sd); n (%).

3.2. Clinical Features

Of the total patients enrolled in the study, 533 (95.9%) were symptomatic [1st wave: n = 223 (93.3%), 2nd wave: n = 209 (96.8%), 3rd wave: n = 101 (100%)]. The median delay in diagnosis was 6 days with an IQR of 9 days - 4 days distributed as follows: 1st and 2nd wave (medians = 6 days; IQR = 9 days - 4 days), 3rd wave (median = 7 days; IQR = 9 days - 4 days). The mean temperature of the global population was 36.7˚C ± 0.73 and 47 (8.8%) had high temperature on the day of admission (T˚C > 38˚C). This hyperthermia was more present in the third wave with a rate of 16%. The main room air saturation was 94% ± 7% and 125 (22.4%) had severe COVID-19 with a room air SaO_2 < 90% on the day of admission. there was a gradual decline during average of SaO_2 at admission over time from 94% ± 6% during the first wave to 92% ± 6% during the second wave and then 90% ± 10% during the third wave. The predominant symptoms remained the same in the three waves of the pandemic and were fatigue, cough and fever, present in more than half of patients for each of these clinical signs (Table 2).

3.3. Laboratory Parameters

In terms of laboratory values, the median rate of CRP in the global study population

Table 2. Clinical characteristics of patients with COVID-19 at the ETC of the DPH (April 2020-September 2021).

Clinical features	Global population N = 556 *	1st wave N = 239 *	2nd wave N = 216 *	3rd wave N = 101 *
Vital signs				
Temperature (˚C)	36.70 ± 0.73	36.77 ± 0.71	36.52 ± 0.67	36.85 ± 0.83
High temperature	47 (8.8%)	22 (9.2%)	9 (4.5%)	16 (16%)
SaO_2 (%)	93 ± 7	94 ± 6	92 ± 6	90 ± 10
SaO_2 < 90%	125 (22.4%)	35 (14.6%)	52 (24.1%)	38 (37.6%)
Symptoms				
Fatigue	321 (58%)	141 (59%)	117 (54%)	63 (62%)
Cough	319 (57%)	139 (58%)	117 (54%)	63 (62%)
Fever	289 (52%)	133 (55.6%)	92 (42.6%)	64 (63.4%)
Arthromyalgia	266 (48%)	110 (46%)	113 (52%)	43 (43%)
Headaches	233 (42%)	115 (48%)	74 (34%)	44 (44%)
Dyspnea	176 (32%)	73 (31%)	67 (31%)	36 (36%)
Ageusia	84 (15.1%)	43 (17.9%)	28 (12.9%)	13 (12.9%)
Anosmia	94 (16.8%)	45 (18.8%)	33 (15.2%)	16 (15.8%)
Sore throat	66 (12%)	38 (16%)	21 (9.7%)	7 (6.9%)
Rhinorrhea	64 (12%)	31 (13%)	24 (11%)	9 (8.9%)

*Mean (m) ± standard deviation (sd); n (%).

was 62 mg/L (IQR = 125 mg/L - 18 mg/L) and positive CRP (>6 mg/L) was noted in 87% of them (369/424). The measurement of d-dimers rate, carried out in 246 patients, showed a median of 360 IU/L (IQR = 1120 UI/L - 174 UI/L) and 26.8% of them had a rate of d-dimers ≥ 1000 IU/L. CRP positivity gradually increased over time with proportions of 70% at the first wave, 83% at the second and 87% at the third wave. As for the dosage of d-dimers, it was only carried out in 4 patients during the first wave, of which the 3 (75%) had a rate ≥ 1000 IU/L. However, this level of d-dimer ≥ 1000 IU/L was found in 31% (28/90) during the third wave and in 23% (35/152) during the second wave.

3.4. Clinical Outcome

The mean duration of hospitalization was 10 days ± 5 days (1st wave: m ± sd = 13 days ± 5 days; 2nd wave: m ± sd = 8 days ± 3 days; 3rd wave: m ± sd = 8 days ± 5 days). Over one month of follow-up time, 41 patients died, *i.e.* a cumulative death rate of 7.4% (**Figure 2**) (1st wave = 6.3% (15/239); 2nd wave = 5.1% (11/216) and 3rd wave = 14.9% (15/216). dead patients were most frequently reported in the first ten days of hospitalization (32, *i.e.* 78% of all death). Twenty-one patients (3.8%) were transferred to intensive care, of whom nine (42.9%) died.

3.5. Risk Factors for Death

3.5.1. Bivariate Analysis

- **Epidemiological factors**

In Log Rank test, the epidemiological risk factors for COVID-19 related death identified were: the third wave of the pandemic, advanced age, presence of at least one comorbidity and high blood pressure (**Figure 3**). The cumulative risk of death was 14.9% in third wave patients versus 6.3% and 5.1% in second and first wave patients, respectively (p = 0.0065). This risk was 11.2% in patients with

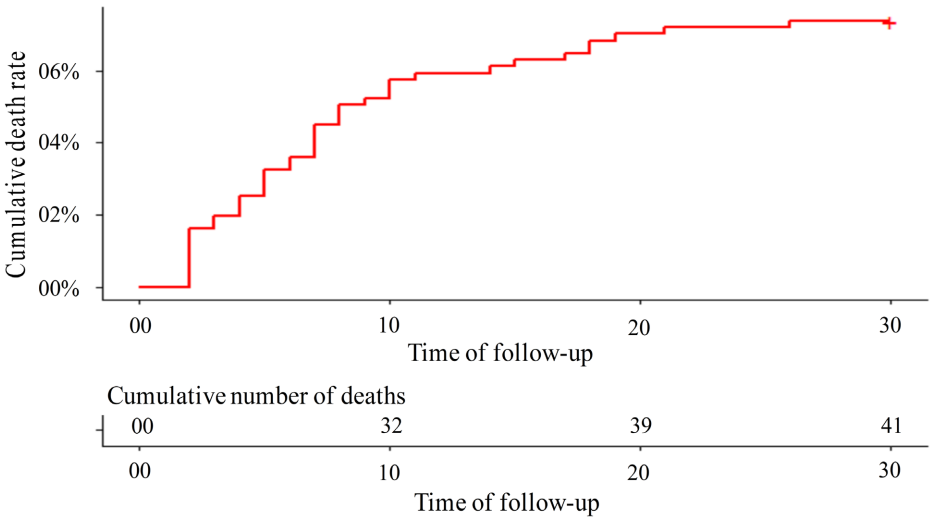

Figure 2. Cumulative death rate of patients with COVID-19 over time of follow-up at the ETC of the DPH (April 2020-September 2021; N = 556).

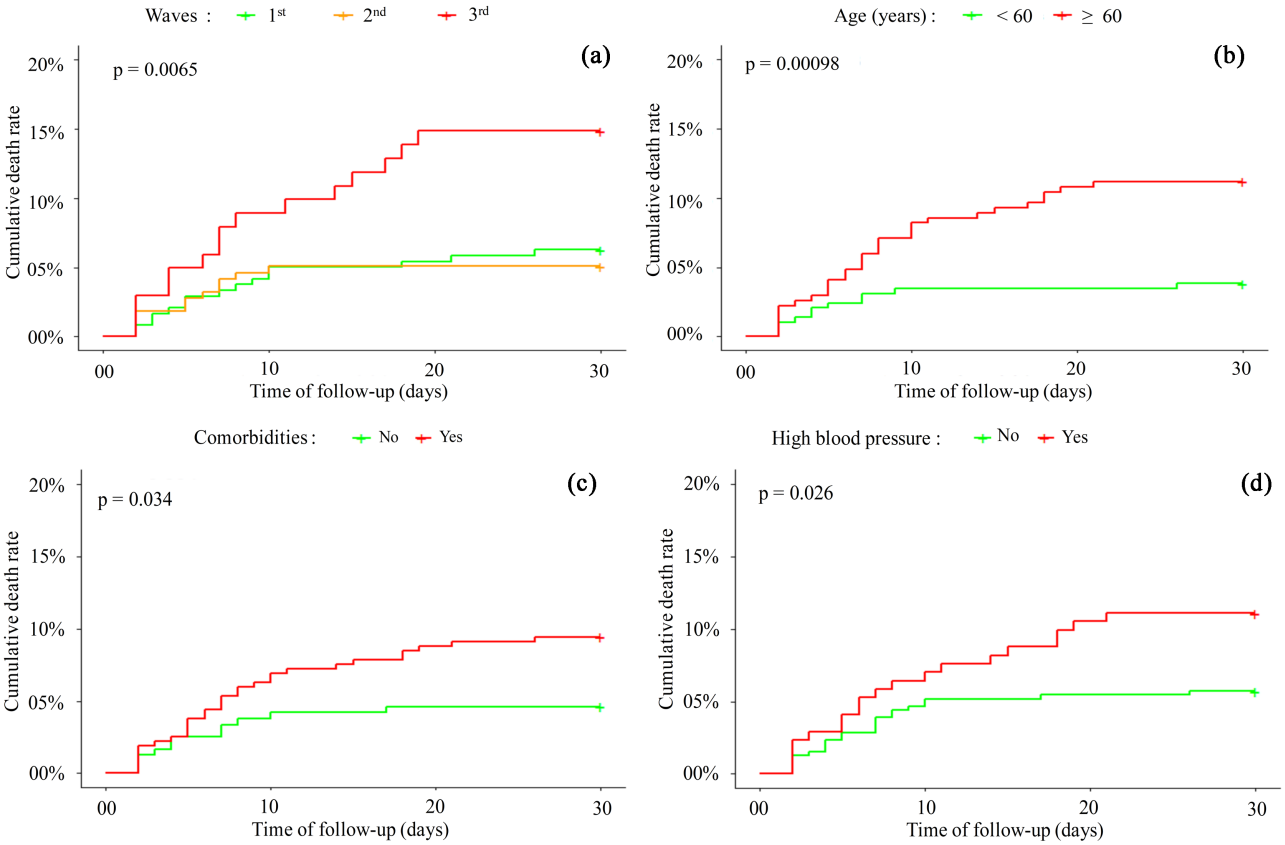

Figure 3. Instantaneous death rate of patients with COVID-19 at the ETC of DPH according to the waves of the pandemic (a), age groups (b), comorbidities (c) and high blood pressure (d) (April 2020-September 2021; N = 556)

60 years of age versus 3.8% in patients under 60 years of age (p = 0.00098). Patients who presented at least one comorbidity appeared to be more at risk to die than those who did not (9.4% vs 4.6%; p = 0.034). Among patients with comorbidities, those with high blood pressure were more likely to die than non-high blood pressure patients (11.1% vs 5.7%, p = 0.026).

- **Biological factors**

In bivariate analysis, COVID-19 patients with CRP rate ≥ 12 mg/L (9.1% vs 1.1%, p = 0.014) as well as those with d-dimer rate ≥ 1000 IU/L (21.2% vs 3.8%, p < 0.0001) were at higher risk to death (Figure 4).

3.5.2. Multivariate Cox Regression

After adjusting for potential confounding variables by multivariate Cox model, advanced age [aHR = 2.6, 95% CI = 1.23 - 5.85, p = 0.013] and third wave of the pandemic [aHR = 2.25, 95% CI = 1.08 - 4.68, p = 0.03] were significant risk factors for COVID-19-related deaths (Table 3). The risk of death in third wave patients was more than 2 times higher than that of the first wave patients. Compared with the second wave, risk of death during the third wave was 3 times higher (aHR = 3.12, 95% CI = 1.41 - 6.92, p = 0.005). Patients over the age of 60 years were 2.7 times more likely to die than patients under the age of 60. Other potential explanatory factors were assessed in this multivariate cox regression

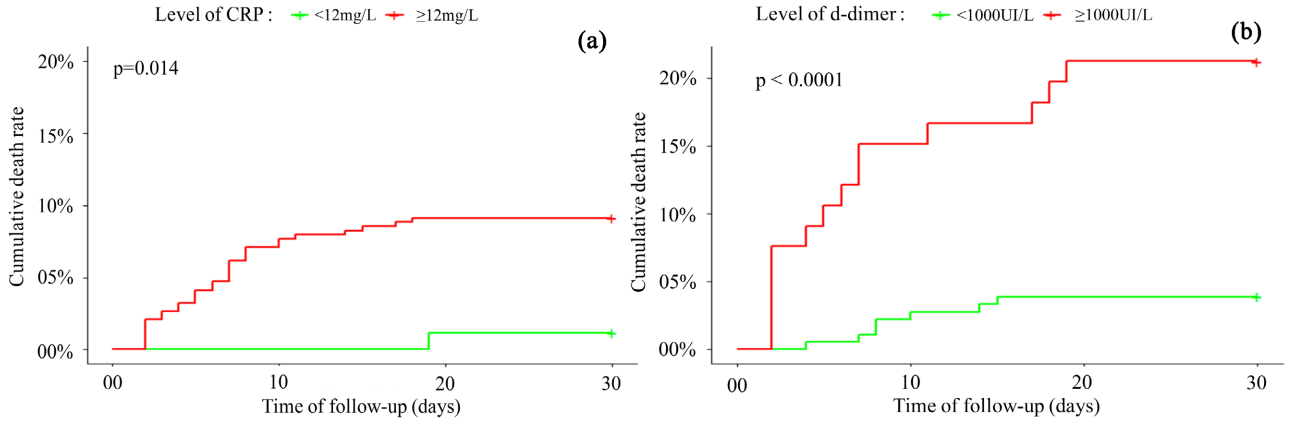

Figure 4. Instantaneous death rate of patients with COVID-19 at the ETC of DPH according to CRP rate ((a); n = 451), and d-dimers rate ((b); n = 446) (April 2020-September 2021; N = 456).

Table 3. Multivariate Cox analysis of risk factors for COVID-19 related death at the ETC of DPH (April 2020-September 2021).

Characteristics	aHR[1]	95% CI[1]	p-value
Waves			
1st	—	—	
2nd	0.72	[0.33, 1.58]	0.4
3rd	2.25	[1.08, 4.68]	0.030
Sex			
Female	—	—	
Males	1.29	[0.66, 2.51]	0.5
Age ≥ 60 years			
No	—	—	
Yes	2.68	[1.23, 5.85]	0.013
Comorbidity			
No	—	—	
Yes	1.29	[0.49, 3.37]	0.6
CPOD			
No	—	—	
Yes	1.00	[0.13, 7.61]	> 0.9
Asthma			
No	—	—	
Yes	1.26	[0.37, 4.35]	0.7
Heart disease			
No	—	—	
Yes	1.33	[0.39, 4.47]	0.6

Continued			
High blood pressure			
No	—	—	
Yes	1.19	[0.54, 2.60]	0.7
Chronic kidney disease			
No	—	—	
Yes	1.44	[0.19, 10.8]	0.7
Obesity			
No	—	—	
Yes	2.72	[0.78, 9.44]	0.12
Diabetes			
No	—	—	
Yes	1.02	[0.48, 2.17]	> 0.9

[1]aHR = adjusted Hazard Ratio, CI = Confidence Interval.

without evidence of significant link with COVID-19 related death.

4. Discussion

In this present prospective survival study including 556 patients with COVID-19 hospitalized at the ETC of the DPH, we first comparatively describe the first three waves of the pandemic. We subsequently determined the cumulative risk of COVID-19 related death over one month of follow-up time for each patient which was 7.4%. The risk factors for death identified in multivariate Cox model were: advanced age (≥60 years) and the third wave of the pandemic. High rates of CRP and d-dimers appeared to be risk factors for COVID-19 related death in bivariate analysis but could not be assessed in the multivariate model due to numerous missing values on these variables. Other Known risk factors for death in the first wave such as hypertension, diabetes or other comorbidities [10] [11] [12] didn't appear to be linked with death in multivariate analysis of our study. This may make us think that there would be fewer differences in terms of death according to the presence or the absence of comorbidities in second and third waves' COVID-19 patients.

4.1. Cumulative Death Rates

The cumulative risk of death during the three waves of the COVID-19 pandemic in this study was 7.4% broken down as follows: 6.3%, 5.1% and 14.9% in the first, second and third waves, respectively. Since the beginning of the pandemic, varied hospital mortality rates have been reported in the literature. Although similar results to ours were found during the first wave in COVID-19 care centers in sub-Saharan Africa such as Sudan and Congo (4.8%) [13], Bissau Guinea and Burkina (5%) [10], higher death rates were noted in other African countries

in that same period such as Gabon (9.8%) [11]. Conversely, in a public COVID-19 care facility in South Africa, a lower cumulative risk of death (2.8%) was found during the first wave of the pandemic [12]. Differences in several points may explain variations noted in hospital mortality of the disease. These may be related to COVID-19 guidelines which were not clearly codified at the start of the pandemic, COVID-19 Care centers performances, COVID-19 severity of in-patients, genetic or socio-cultural characteristics. However, evidence suggests that risk of hospital death from the disease seemed to be higher in developed countries. In a Mexican study conducted in a COVID-19 care facility on March 2020, a mortality rate of 10.33% was noted [14]. In France, one out of five patients hospitalized for this infection died during the first wave [15]. This confirms the epidemiological trend according to which there is significantly a lower morbidity and mortality burden of COVID-19 in Africa. This scenario could be mainly in link with the fact that the African population is much younger, with a lower rate of non-communicable comorbidities. Dry weather in most of the African countries, not in favour of the virus survival is also mentioned by some authors as a hypothesis [16].

4.2. Risk Factors

- **The third wave of COVID-19**

In our study, patients from the 3rd wave of the pandemic were over 2 times more likely to die than those from the first wave. This risk was 3 times higher than that of second-wave patients. The third wave of the pandemic in Senegal, as in many other African countries, corresponded to the predominant circulation of delta variant of SarsCov2 which is known worldwide to be the most contagious and fatal variant. In a study conducted in Algeria, Touahri R *et al.* underlined that mortality rate of COVID-19 patients from the third wave (corresponding to the delta variant of SarsCov2) was significantly higher than that of the first two waves (18% versus 3%, $p < 0.001$) [17]. Similar result was demonstrated by Bast E *et al.* in the United States among not vaccinated patients with a risk of delta variant related death which was multiplied by 2 compared to patients from the pre-delta period [18]. In fact, delta variant (B.1.617.2) presents 23 mutations out of which 12 relate to the protein spike (S) of SarsCov2. S Protein allows the virus to bind to the ACE2 receptors and also is the target of the host immune system. Mutations in this S protein therefore facilitate its rapid replication and its immune escape [19]. These two events could explain the severity and increased mortality of patients infected with delta variant of the virus. In addition, the rate of patients' admissions to COVID-19 care centers in Senegal was much higher during the third wave with a rapid saturation of hospital beds. This was the cause of exhaustion of medical staff and problems in transferring severe cases to dedicated intensive care units.

- **Advanced age**

Our study shows that patients older than 60 years of age were 2.7 times more

at risk to die than patients under 60. In most studies, both in Africa and on other continents, advanced age represents the leading risk factor of death in COVID-19 patients. A similar link has already been underlined in a multicentre study in Senegal during the first wave of the pandemic [20]. Kombila UD *et al.* in Gabon showed that patients with COVID-19 aged over 65 were at higher risk of dying than patients under 65 (OR = 4.632; 95% CI [2.243 - 9.565]; p < 0.001) [12]. Similarly, in a multicentre study conducted in Guinea and Burkina Faso, COVID-19 patients older than 60 died significantly more than patients under 60 (OR = 2.9; 95% CI [1.7 - 4.8]) [11]. Chiquete E, *et al.* had identified in Mexico that age over 40 was the first epidemiological risk factor for death in patients with COVID-19 (HR = 4.21; 95% CI [3.59 - 4.93]) [14]. This same trend was reported in China by Zhang Y *et al.* in patients over 80 years old with COVID-19 (HR = 12.58; 95% CI [6.78 - 23.33]) [21]. The link between advanced age and occurrence of death is easily explained by the weakness of the immune system and the higher rate of comorbidities in the elderly, which make them more vulnerable to this infection.

- **High rates of CRP and d-dimers**

Even though biological parameters were not taken into account in the multivariate Cox regression due to the high number of missing values on these variables, bivariate analysis showed that the risk of death was increased by CRP rate ≥ 12 mg/L (9.1% vs 1.1%, p = 0.014) and d-dimer rate ≥ 1000 IU/L (21.2% vs 3.8%, p < 0.0001). Similar results were found by French authors. Nancy's medical staff showed that a high level of d-dimers at the day of admission (HR = 3.6 [1.1 - 12.3]; p = 0.037)) or an initially low level of d-dimers with a rapid increase during hospitalization (HR = 18.1; [4.3 - 76.2], p < 0.0001) increased the risk of death in patients with COVID-19 [22]. In Dijon, Sixt T *et al.* found that patients hospitalized for COVID-19 with a worseness of the disease had a significantly higher CRP rate (average 127 mg/L vs 80.3 mg/L, p < 0.001) [23]. However, it has been shown by other authors that an increased CRP rate may not be a reliable indicator of COVID-19 severity [24]. D-dimers are degradation products from fibrin which can testify to frequent thromboembolic events in patients with COVID-19, often cause of death. They are also, as well as CRP, non-cytokine inflammatory parameters that are highly produced in severe and critical COVID-19 [25].

4.3. Limitations of the Study

Despite the results globally corroborate literature data, this study presents a number of limitations. Firstly, it was conducted in a single COVID-19 care center in Senegal. That didn't allow a statistical inference. Secondly, routine biological parameters measurements such as CRP and d-dimers were not carried out consistently during the first wave of the pandemic because of biosafety fear of blood samples. We were therefore unable to assess these two potentially explanatory biological parameters for death in the multivariate model, due to a

high number of missing values for these variables. Finally, even if there was a predominant presence of beta and delta variants of Sars-Cov2 during the second and third waves respectively, this predominance varied from one area to another. It may then be difficult to compare our results with other reported data in the literature according to the order of waves.

5. Conclusion

Our study showed that patients with COVID-19 who were elderly or infected during the third wave of the pandemic had an increased risk of death. high rate of CRP and d-dimer may also be risk factors for death in these patients. It is therefore necessary to take into account these prognosis factors of death for a better management of COVID-19 in-patients.

Acknowledgements

We would like to acknowledge:

Mr. Mor Diandam DIOP (English Professor at Darou Nahim high school, Senegal) for his help in the English translation of the manuscript.

Mrs. Richlove Konadu Afoakwa (Ghana Police Service, Accra, Ghana) for the language edits.

We acknowledge all the members of the ETC healthcare team at the military principal hospital of Dakar for their involvement in the medical care of patients.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] World Health Organization (2020) Novel Coronavirus (2019-nCoV): Situation Report 10. https://apps.who.int/iris/handle/10665/330775

[2] Nachega, J., Seydi, M. and Zumla, A. (2020) The Late Arrival of Coronavirus Disease 2019 (COVID-19) in AFRICA: Mitigating Pan-Continental Spread. *Clinical Infectious Diseases*, **71**, 875-878. https://doi.org/10.1093/cid/ciaa353

[3] World Health Organization (2020). WHO Director-General's Opening Remarks at the Media Briefing on COVID-19—11 March 2020. https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020

[4] World Health Organization (2022) WHO Coronavirus (COVID-19) Dashboard. https://covid19.who.int/

[5] Organisation Mondiale de la Santé (OMS) (2022) Prise en Charge Clinique de la COVID-19: Orientations éVolutives, Genève. https://apps.who.int/iris/bitstream/handle/10665/363044/WHO-2019-nCoV-Clinical-2022.1-fre.pdf

[6] Desvaux, É. and Faucher, J.F. (2020) Covid-19: Aspects Cliniques et Principaux éléments de Prise en Charge. *Revue Francophone des Laboratoires*, **2020**, 40-47. https://doi.org/10.1016/S1773-035X(20)30312-9

[7] Diop, M., Ba, P.S., Lo, M., Essomba, N., Fall, B., Sarr, M.N., Ndiaye, M., Wembulua, B., Mbaye, N.F.K., Lakhe, N.A., Fall, B., Niang, A., Diallo-Mbaye, K., Fortès, L., Faye, O., Dia, N., Ndiaye, A.R., Seydi, M., Sall, A.A. and Dieng, M.T. (2021) Factors Associated with Severe COVID-19 in an Epidemic Treatment Center at Dakar. *Journal of Infectious Disease and Epidemiology*, **7**, Article 203.

[8] Utulu, R., Ajayi, I.O., Bello, S., Balogun, M.S., Madubueze, U.C., Adeyemi, I.T., Omoju, O.T., Adeke, A.S., Adenekan, A.O. and Iyare, O. (2022) Risk Factors for COVID-19 Infection and Disease Severity in Nigeria: A Case-Control Study. *The Pan African Medical Journal*, **41**, Article 317. https://doi.org/10.11604/pamj.2022.41.317.34307

[9] Ngomas, J.F., PC, N.O., Nyangui, D.E.M., Manga, F., Bitegue, L., Igala, M. and Essola-Rerambiah, L. (2022) Aspects Epidémiologiques et Facteurs de Mauvais Pronostic des Patients Atteints de COVID-19 Admis en Réanimation au Centre Hospitalier Universitaire de Libreville au Cours des Trois Premières Vagues de la Pandémie. *Health Sciences and Disease*, **23**, 1-7.

[10] Jaspard, M., Sow, M.S., Juchet, S., Dienderé, E., Serra, B., Kojan, R., Poda, A., Keita, S., Anglaret, X. and Malvy, D. (2021) Présentation clinique, survie et facteurs associés à la mortalité: Une étude prospective dans trois centres COVID-19 en Afrique de l'Ouest. *Infectious Diseases Now*, **51**, S59. https://doi.org/10.1016/j.idnow.2021.06.125

[11] Kombila, U.D., Boulingui, C.M., Igala, M., Ngomas, J.F., Bivigou, E.A., Makao, A.I., Massolo, R., Kouna, P., Bouyou Akote, M. and Boguikouma, J.B. (2022) Évolution clinique et facteurs pronostiques de décès des patients infectés par le SARS-CoV-2, hospitalisés en secteur d'infectiologie COVID du centre hospitalier et universitaire (CHU) de Libreville, Gabon. *Revue des Maladies Respiratoires Actualités*, **14**, 139-140. https://doi.org/10.1016/j.rmra.2021.11.211

[12] Western Cape Department of Health and National Institute for Communicable Diseases of South Africa (2020) Risk Factors for Coronavirus Disease 2019 (COVID-19) Death in a Population Cohort Study from the Western Cape Province, South Africa. *Clinical Infectious Diseases*, **73**, e2005-e2015.

[13] Leidman, E., Doocy, S., Heymsfield, G., Sebushishe, A., Mbong, E.N., Majer, J., The IMC-CDC COVID-19 Research Team and Bollemeijer, I. (2022) Risk Factors for Hospitalization and Death from COVID-19: A Prospective Cohort Study in South Sudan and Eastern Democratic Republic of the Congo. *BMJ Open*, **12**, e060639. https://doi.org/10.1136/bmjopen-2021-060639

[14] Chiquete, E., Alegre-Díaz, J., Ochoa-Guzmán, A., Toapanta-Yanchapaxi, L.N., González-Carballo, C., Garcilazo-Ávila, A., Santacruz-Benitez, R., Ramírez-Reyes, R., Wong-Chew, R.M., Guerrero, G., Schmulson, M., Berumen, J., Sandoval-Rodríguez, V., Ruiz-Ruiz, R. and Cantú-Brito, C. (2022) Ethnicity and Other COVID-19 Death Risk Factors in Mexico. *Archives Medical Science*, **18**, 711-718.

[15] Semenzato, L., Botton, J., Drouin, J., Cuenot, F., Dray-Spira, R., Weill, A. and Zureik, M. (2021) Maladies chroniques, états de santé et risque d'hospitalisation et de décès hospitalier pour COVID-19: Analyse comparative de données des deux vagues épidémiques de 2020 en France à partir d'une cohorte de 67 millions de personnes. Rapport EPI-PHARE-Groupement d'intérêt scientifique (GIS) ANSM-CNAM. https://www.epi-phare.fr/app/uploads/2021/07/epi-phare_risques_hospitalisations_deces_covid19_20210721.pdf

[16] Hardy, É.J. and Flori, P. (2021) Spécificités épidémiologiques de la COVID-19 en Afrique: préoccupation de santé publique actuelle ou future? *Annales Pharmaceutiques Françaises*, **79**, 216-226. https://doi.org/10.1016/j.pharma.2020.10.011

[17] Touahri, R., Bourboune, A., Kaouane, H., Issoulah, S., Aouinate, S. and Ketfi, A. (2022) Étude comparative du profil clinicobiologique et évolutif entre la 3e vague et 1-2e vague de COVID-19 dans un service hospitalier de pneumologie. *Revue des Maladies Respiratoires Actualités*, **14**, 128. https://doi.org/10.1016/j.rmra.2021.11.184

[18] Bast, E., Tang, F., Dahn, J. and Palacio, A. (2021) Increased Risk of Hospitalization and Death with the Delta Variant in the USA. *The Lancet Infectious Diseases*, **21**, 1629-1630. https://doi.org/10.1016/S1473-3099(21)00685-X

[19] Shiehzadegan, S., Alaghemand, N., Fox, M. and Venketaraman V. (2021) Analysis of the Delta Variant B.1.617.2 COVID-19. *Clinics and Practice*, **11**, 778-784. https://doi.org/10.3390/clinpract11040093

[20] Diarra, M., Barry, A., Dia, N., Diop, M., Sonko, I., Sagne, S. and Senegalese District Medical Officers (2022) First Wave COVID-19 Pandemic in Senegal: Epidemiological and Clinical Characteristics. *PLOS ONE*, **17**, e0274783. https://doi.org/10.1371/journal.pone.0274783

[21] Zhang, Y., Luo, W., Li, Q., Wang, X., Chen, J., Song, Q., Tu, H., Ren, R., Li, C., Li, D., Zhao, J., McGoogan, J.M., Shan, D., Li, B., Zhang, J., Dong, Y., Jin, Y., Mao, S., Qian, M., Lv, C., Zhu, H., Wang, L., Xiao, L., Xu, J., Yin, D., Zhou, L., Li, Z., Shi, G., Dong, X., Guan, X., Gao, G.F., Wu, Z. and Feng, Z. (2022) Risk Factors for Death among the First 80 543 Coronavirus Disease 2019 (COVID-19) Cases in China: Relationships between Age, Underlying Disease, Case Severity, and Region. *Clinical Infectious Diseases*, **74**, 630-638. https://doi.org/10.1093/cid/ciab493

[22] Julien, M., Omorou, Y., Dufrost, V., Foret, T., Broseus, J., Salignac, S., Wah, D., Eschwège, V. and Zuily, S. (2022) La cinétique des D-dimères pendant l'hospitalisation est un facteur pronostique majeur de décès chez les patients hospitalisés pour COVID-19. *Revue d'Épidémiologie et de Santé Publique*, **70**, S83. https://doi.org/10.1016/j.respe.2022.03.114

[23] Sixt, T., Moretto, F., Abdallahoui, M., Chavanet, P., Devilliers, H., Catherine, F. and Piroth, L. (2020) COVID-19: Une cohorte descriptive de 222 patients hospitalisés. *Médecine et Maladies Infectieuses*, **50**, S62-S63. https://doi.org/10.1016/j.medmal.2020.06.120

[24] Ferrari, D., Motta, A., Strollo, M., Banfi, G. and Locatelli, M. (2020) Routine Blood Tests as a Potential Diagnostic Tool for COVID-19. *Clinical Chemistry and Laboratory Medicine* (*CCLM*), **58**, 1095-1099. https://doi.org/10.1515/cclm-2020-0398

[25] Muller, M., Bulubas, I. and Vogel, T. (2021) Les facteurs pronostiques dans la Covid-19. *NPG Neurologie-Psychiatrie-Gériatrie*, **21**, 304-312. https://doi.org/10.1016/j.npg.2021.06.002