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ORIGINAL RESEARCH

Clinical Characteristics and Mortality Trends Among COVID-19 Patients During the First Four Waves in Ngaliema Clinic, Democratic Republic of the Congo

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Background: COVID-19 disease has been a deadly pandemic in different waves in the Democratic Republic of Congo. However, knowledge of the clinical characteristics of COVID-19 patients and the factors associated with death during different waves is important.

Methods: We conducted a retrospective cohort of 410 patients hospitalized during 4 waves of COVID-19, from March 20, 2020, to January 2, 2022, at the Ngaliema clinic in DR Congo. We included any patient hospitalized for COVID-19 with biological confirmation by RT-PCR. Factors associated with death were investigated using logistic regression.

Results: During the 4 waves of the COVID-19 pandemic at Clinique Ngaliema, complaints on admission were most often fever, cough and physical asthenia. Death was most common in the elderly, hypertensive and diabetic patients, those with elevated CRP and hyper leukocytosis. Mortality was highest in the 1st wave (28%), followed by the 3rd wave (27%), then the 2nd (22%) and 4th waves (21%). Factors associated with death were hyper leukocytosis (ORa: 2.76; CI 95%: 1.25–6.1), severe disease stage (ORa 21.24; CI 95%: 1.87–24). Vitamin C 500 mg twice a day use was protective (ORa: 0.24; CI 95%: 0.08–0.72).

Conclusion: COVID-19 disease poses a real public health problem, with non-negligible mortality. Factors associated with death were degree of disease severity, hyper leukocytosis and non-use of vitamin C. Taking these factors into account will help clinicians and decision-makers to anticipate future waves of the pandemic.

Keywords: clinical characteristic, COVID-19, mortality, Democratic Republic of Congo

Background

Coronavirus diseases 2019 (COVID-19) are a pandemic that has caused thousands of deaths worldwide, and the African continent has not been spared.[1] The first wave was particularly severe, disrupting the healthcare system and swamping hospitals and intensive care units. The outbreak of COVID-19 showed that most countries were unprepared and had insufficient resources to deal with this virus. Compared to other continents such as Europe, Asia and America, in many African countries, there was a lack of emergency department beds, resuscitation department beds, oxygen production plants, artificial respirators and even personal protective equipment for front-line providers.[2] A number of factors influence the timing and impact of waves on public health, including natural and vaccine-induced immunity, seasonality, and the types and characteristics of SARS-COV-2 variants.[3]

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In contrast to the first wave, when data on COVID-19 was limited, scientific understanding in subsequent waves improved markedly, and the healthcare system was strengthened as a result. The experience gained during the first wave, in particular, the large number of scientific publications identifying mortality risk factors, and testing types of respiratory assistance equipment and different drugs including antivirals, immunomodulators, corticoids etc, enabled providers to better prepare to fight the pandemic during subsequent waves with great mastery.[4] Furthermore, strong anti-oxidant and anti-inflammatory properties of vitamin C lower the risk of tissue damage from oxidative stress and inhibit the cytokine storm, an excessive inflammatory response. By boosting interferon synthesis and lymphocyte proliferation, vitamin C enhances the host antiviral immune response.[5]

Many of the differences between waves can be attributed to the ability of SARS-CoV-2 to mutate and produce characteristics that favor increased transmissibility and immune evasion.[6,7]

In sub-Saharan Africa, the evolution of average case fatality rate in the 4 waves is 2.5% to 3.5% for the first wave, 3.0% to 4.5% for the second wave, 4% to 6% for the third wave and 0.5% to 1.5% for the fourth wave.[8–11]

In the Democratic Republic of the Congo (DRC), despite numerous vaccination efforts, the country has had one of the lowest vaccination rates in the world in the fight against COVID-19. Only 0.87% of the DRC's population has received even one dose of vaccine, whereas the country has received 8.2 million doses of vaccine against COVID-19, but especially with the appearance of the Indian variant in 2021, the Congolese population in general and Kinshasa in particular is refusing to be vaccinated and, above all, to be screened.[12] Among SARS-CoV-2, B.1.1.7 (alpha), B.1.351 (beta), B.1.617.2 (delta), and B.1.1.529 (Omicron) were among the variant of concern (VOCs) that caused the most controversy during the global COVID-19 epidemic. While labs in Europe, America, and many Asian nations were able to identify VOCs and VOIs throughout several pandemic waves, most hospitals in sub-Saharan Africa (SSA) were unable to access this data due to a lack of laboratory resources.[13] In a single center study in the DRC, the Omicron in the fourth wave, the Delta VOC was primarily represented in the third wave. In relation to the total number of patients that tested positive (both hospitalized and non-hospitalized), the hospitalized patient count and the proportion of deaths were 215 and 21% for the first wave, 196 and 7% for the second wave, 254 and 16% for the third wave, and 178 and 7% for the fourth wave.[14]

In the DRC, a few studies have described the epidemiological and clinical profile and identified factors associated with mortality. Most of these studies were carried out during the first wave.[15–18] After a series of 6 waves of COVID-19 pandemics in the DRC, the first four waves recorded several cases and deaths.[19] But few studies have described clinical characteristics and the comparative mortality of patients during these first four waves, which justifies the present study. The general aim of the present study is to describe the clinical characteristics of COVID-19 patients during the first 4 waves at the Ngaliema clinic and to identify factors associated with mortality during the first 4 waves at the Ngaliema clinic.

Methods

Design and Period of Study

The present retrospective cohort study focused on the medical records of patients who tested positive for COVID-19 and were hospitalized. It covered the period from March 10, 2020, to January 2, 2022.

Study Setting

The present study was conducted at the Ngaliema Clinic. Ngaliema Clinic is located in Kinshasa, capital of the Democratic Republic of the Congo. It is one of the capital's major medical facilities and is classified by the World Health Organization as one of the country's reference hospitals, as well as for Central Africa. Established in 1927, it is currently a national tertiary referral hospital. Ngaliema Clinic has a capacity of 254 real beds and over 320 budgetary beds. The DRC's COVID-19 response organization states that COVID-19 treatment facilities and health zones are where COVID-19 patients are managed at the provincial level. The health zone manages asymptomatic patients, and patients may be referred to COVID-19 treatment centers according on the severity of their symptoms after receiving a fragility score. Mild, moderate, severe or critical patients are addressed in the COVID-19 treatment centers. There was 35 health

zones and 14 COVID-19 treatment facilities in Kinshasa. Ngaliema Clinic was the main COVID-19 treatment facility in the west of Kinshasa.

Study Population

Patients meeting the following criteria were included in the study:

Inclusion Criteria

Any patient hospitalized for COVID-19 with biological confirmation by RT-PCR. The nasopharyngeal swab was used as the sample.

Data Collection

All data were collected from hospitalized patients' records, selected on the basis of the date of admission and taking into account our inclusion and exclusion criteria. Data were transcribed anonymously onto a pre-established individual survey form. The data collected were: Sociodemographic data (age, sex), comorbidities (arterial hypertension, diabetes mellitus, chronic renal disease, sickle cell disease, HIV), symptoms on admission, length of hospital stay, origin, examination data in admission (Blood pressure, saturation, severity), biological data (CRP, white blood cell count, blood glucose, hemoglobin), treatment (vitamin C, antibiotics, anticoagulant, dexamethasone, oxygen). Blood glucose is classified as low, normal or high. Hemoglobin is classified as low, moderate or normal, and vitamin C as received or not received. The survey form was completed by the authors. Data collection was standardized using a predefined electronic form. Operational definitions were based on WHO criteria for COVID-19. To reduce inter-observer variability, the following steps were implemented: Firstly, pre-training, during which investigators attended a 4-hour session on data collection protocols. Secondly, a Coding Guide in which a manual detailing data entry rules was distributed, and thirdly, a random audit in which 10% of the files were re-analyzed by a second independent observer.

Operational Definitions

Classification of COVID-19 According to Severity

Table 1 describes the characteristics of mild, moderate, severe and critically COVID-19 according to WHO.[20]

The frailty score was used for moderate or light covid patients with risk factors. This score helped in deciding hospitalization, especially when The score was ≥5 (moderate frailty) with Increased Risk of worsening and ≥7 (severe frailty) with Risk of Death 2x more likely.[21]

Inpatients

In accordance with the national management guidelines, patients admitted to COVID-19 treatment centers were those with moderate, severe and critical COVID-19, or with both mild COVID-19 and risk factors for severe disease.[22]

Defining COVID-19 Waves in the DRC

According to the WHO's definition of COVID-19 waves, from March 9, 2020, through January 2, 2022, the following periods have been considered as the 4 waves in our country:[19]

Table 1 The WHO Clinical Classification of the COVID-19[14]

Mild Case	Moderate	Severe	Critically Severe
Mild clinical manifestations, no imaging performed	Fever, dyspnea, Appearance of pneumonia on Xray or CT	Meet any of the following: Respiratory distress, RR ≥ 30/min Oxygen saturation ≤ 93% PaO2/FiO2 ≤ 300 mmHg	Respiratory failure requiring enhanced respiratory support, which may be combined with shock or other organ dysfunction, patients need intensive care monitoring and treatment

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- 03/09/2020– 08/23/2020 = first wave
- 08/24/2020– 04/04/2021 = second wave
- 04/05/2021– –08/15/2021 = third wave
- 08/16/2021–01/02/2022 = fourth wave

Treatment According National Guideline in Democratic Republic of the Congo

Mild and moderate forms of COVID-19 were treated with chloroquine 250 mg twice daily and azithromycin 500 mg once on the first day, then 250 mg daily for 4 days. For moderate cases, prophylactic anticoagulation was added. Cases of severe or critical COVID-19 were treated with the same regimen as for mild and moderate forms, but anticoagulation was given at a therapeutic dose. Dexamethasone at a dose of 6mg/d IV was given in all cases of severe and critical COVID-19. All forms received symptomatic treatment, with antipyretics in case of fever, and vitamin C 500 mg twice a day in all cases. Oxygen therapy (nasal tube or mask) was recommended in cases of oxygen desaturation. In some patients, non-invasive or invasive ventilation was recommended. Antibiotics, rehydration and correction of hydro-electrolytic disorders were also recommended.[22] Therapies like anticoagulant, vitamin C and dexamethasone were not used in some cases because of resource limitations or clinical decisions.

Statistical Analysis

Data were entered and coded using Excel 2010. Data analysis was performed using Epi info software version 2.2.3/0. Before to do analysis, we transformed the variables of age, duration of symptoms before consultation, Mean arterial pressure (MAP), C reactive protein (CRP), leukocytes, glycemia and hemoglobin into categorical variables. The statistics used to describe the variables were mean ± standard deviation for symmetrically distributed continuous quantitative variables. Qualitative variables were described as relative (%) and/or absolute (n) frequencies. Clinical manifestations are presented as bar charts. Proportions were compared using the chi-square test, means were compared using the Student's *t*-test, and logistic regression was used to search for factors associated with COVID-19. The strength of association was assessed by calculating the Odds Ratio and its 95% confidence interval in bivariate and multivariate analysis. A multivariate logistic regression model was developed to estimate adjusted Odds ratios (aOR) adjusting for all factors significant in the bivariate analysis. The multivariate logistic regression was adjusted for the following variables: age, sex, origin, comorbidities (DM, HTN), CRP, leukocytes, severity, treatment (use of vitamin C, use of anticoagulant, use of dexamethasone). The value of $P < 0.05$ was the threshold of statistical significance. The data have been illustrated in tables and figures.

Ethical Considerations

Data collection, recording and statistical analysis were kept anonymous in order to respect confidentiality. None of the procedures used in this study were harmful to the participants. Patients gave their consent before taking part in the study. The investigators conducted this study taking into account the principles of the Declaration of Helsinki and its subsequent relevant amendments. Written consent was obtained for patients. The study was approved by the University of Kinshasa School of Public Health 'Ethics committee (ESP/CE/179/2020).

Results

General Characteristics of Inpatients at Ngaliema Clinic

During the study period, 410 patients were hospitalized for COVID-19. Among hospitalized patients, 109 (27%) deceased. More men died than women (65%). Patients aged 60 or over died more than those under 60. Diabetics and hypertensives died more than patients without diabetes mellitus or hypertension. Patients with chronic kidney disease, COPD, HIV infection and sickle cell disease did not have higher mortality. Transferred patients died more than those from home (Table 2).

Table 2 General Characteristics of Patients Hospitalized for COVID-19 at Clinique Ngaliema

Variable	Deceased n = 109 n (%)	Survivor n = 301 n (%)	P
Sociodemographic characteristics			
Sex			
Male	71(29.6)	169(70.4)	0.05
Female	38(22.4)	132(77.6)	
Age			
<60 years	49(20.6)	189(79.4)	0.00
≥60 years	60(34.9)	112(65.1)	
Comorbidities			
HTN			
Yes	28(25.7)	119(39.5)	0.000
No	81(74.3)	182(60.5)	
Diabetes mellitus			
Yes	51(46.8)	60(19.9)	0.000
No	58(53.2)	241(80.1)	
CKD			
Yes	7(6.4)	10(3.3)	0.09
No	102(93.6)	291(96.7)	
HIV			
Yes	1(0.9)	5(1.7)	
No	108(96.4)	296(98.3)	0.325
COPD			
Yes	2(1.8)	1(0.03)	
No	107(98.2)	300(99.07)	0.096
Drepanocytosis			
Yes	3(2.8)	8(2.7)	0.461
No	106(97.2)	293(97.3)	
Duration of symptoms			
Before admission			
≤48 h	3(3.0)	11(4.1)	0.325
>48	98(97.0)	257(95.9)	
Undeterminate (41)			
Origin			
Residence	52(47.7)	207(66.8)	0.000
Transferred from centers	57(52.3)	94(32.2)	

Note: Vaccination status and variants are unknown.
Abbreviations: HTN, hypertension; CKD, chronic kidney disease; COPD, chronic Obstructive pulmonary diseases; HIV, Human immunodeficiency virus.

Clinical, Biological and Therapeutic Manifestations of Patients Hospitalized at the Ngaliema Clinic

Symptoms on Admission

Figure 1 shows that cough followed by physical asthenia, fever and dyspnea constitute the clinical tetrad of patients hospitalized for COVID-19. The same pattern of the 4 predominant signs is found in all waves.

Physical Examination, Biological and Therapeutic Data

The majority of patients who died had a MAP between 65 and 130 mmHg. The majority of deceased patients were admitted with an oxygen saturation of less than 90%. A large number of patients were admitted in the severe stage, and severe cases died more than moderate and mild cases. First-wave patients were more numerous than other waves, and

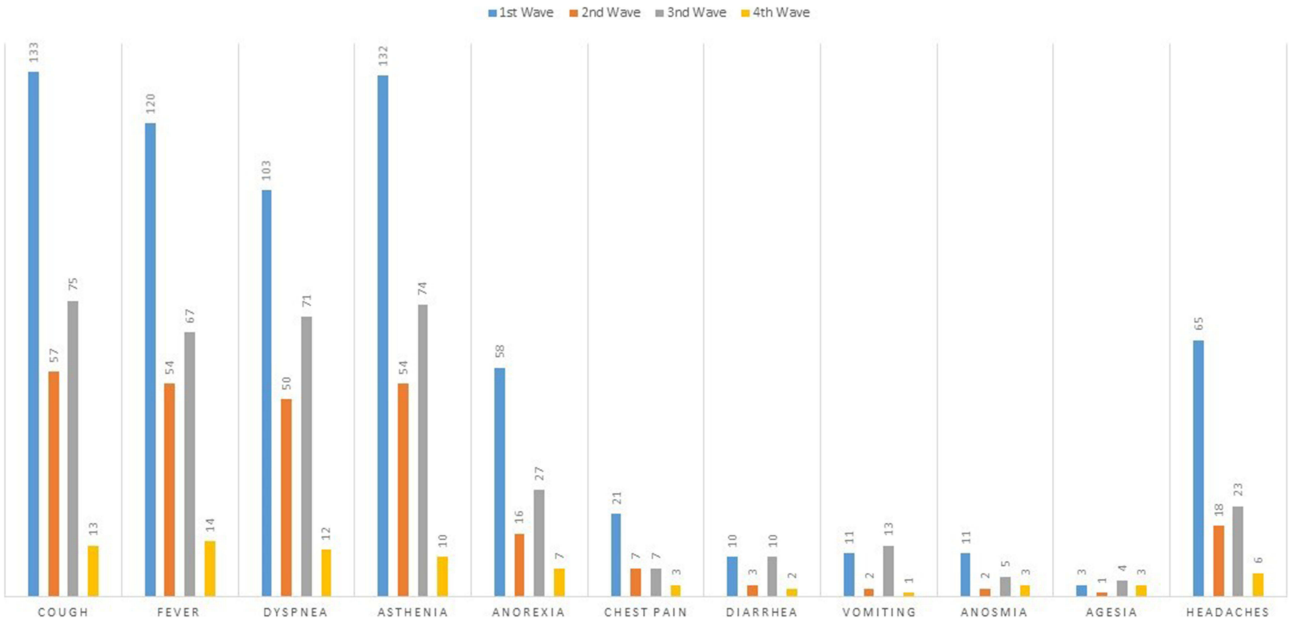

Figure 1 Distribution of symptoms across waves.

mortality was highest in the first wave, followed by the third, second and fourth waves. Biologically, death was significantly linked to a disturbance in inflammatory biology (increased CRP and hyper leukocytosis); deceased patients had CRP ≥ 100 mg/l, WBC ≥ 10000/mm3. Although the difference was not significant, the majority of patients who died had hyperglycemia, and a hemoglobin level ≥ 7. Death was significantly associated with failure to take vitamin C, dexamethasone, oxygen therapy and anticoagulants (Table 3).

Table 3 Distribution of Cases by Physical Data, Waves, Biological Parameters and Therapeutic Means

Variable	Deceased n = 109	Survivor n= 301	P
Physical data			
MAP			
<65 mm Hg	3(2.9)	3(1.0)	0.000
65–130 mm Hg	89(87.3)	278(97.2)	
>130 mm Hg	10(9.8)	5(1.7)	
Sa02			
<90%	82(75.9)	93(68.2)	0.000
≥90%	26(24.1)	199(31.8)	
Severity			
Mild	3(1.9)	152(50.5)	0.000
Moderate	5(4.6)	69(22.9)	
Severe	101(92.7)	80(26.6)	
Wave			
1ère wave	60(55)	154(51.4)	
2e wave	17(15.6)	59(19.6)	0.795
3e wave	28(25.7)	75(24.9)	
4e wave	4(3.7)	13(43)	

(*Continued*)

Table 3 (Continued).

Variable	Deceased n = 109	Survivor n= 301	P
Biological data			
CRP			
<100 mg/l	18(38.7)	81(66 0.4)	0 0.000
≥100 mg/l	29(61.3)	41 (33.6)	
Undeterminate (243)	72	179	
White blood cell count (elements/mm3)			
<4000/mm3	3(5.5)	13 (9.7)	
4000–10000/mm3	15 (27.3)	74(552)	0.000
≥10000/mm3	37(67.3)	47(35.1)	
Occasional capillary blood glucose (mg/dl)			
<60	2(5.9)	5(9.0)	
60–200	22(64.7)	36(65.5)	0.819
≥200	10(64.4)	14(255)	
Undeterminate	75	246	
Hemoglobin (g/dl)			
<7	4(8.2)	7(5.3)	
≥7	45(91.8)	125(94.7)	0.245
Undeterminate	60	169	
Therapeutic means			
Vitamin C			
Yes	35 (32.1)	150(45.1)	0.000
No	74(67.9)	151(54.9)	
Dexamethasone			
Yes	13(11.9)	57(18 0.9)	0.047
No	96(88.1)	244(81.1)	
Oxygen therapy			
Yes	9(8.3)	145(48.2)	0.000
No	100(91,7)	156(51.8)	
Anticoagulant			
Yes	8(7.3)	63(20.7)	0,000
No	101(92.7)	238(79.3)	
Antibiotic therapy			
Yes	72(66.1)	186(61.8)	0.217
No	37(33.9)	115(38.2)	

Abbreviations: MAP, Mean arterial pressure; CRP, C reactive protein; SaO2, oxygen saturation.

Mortality Rate and Factors Associated with Death

Looking at this histogram, we can see that the 1st wave had more cases (214 hospitalized patients), of which 28% were deaths, followed by the 3rd wave with 103 cases, of which 27% were deaths, then followed by the 2nd and 4th wave (Figure 2).

In multivariate analysis, we observed that hyper leukocytosis above 10,000/mm3 (aOR: 2.76; CI 95%: 1.25–6.1), severe COVID-19 (aOR: 21.24; CI 95%: 1.87–24) and non-use of vitamin C (aOR: 0.24; CI 95%: 0.08–0.72) were the only risk factors associated with death (Table 4).

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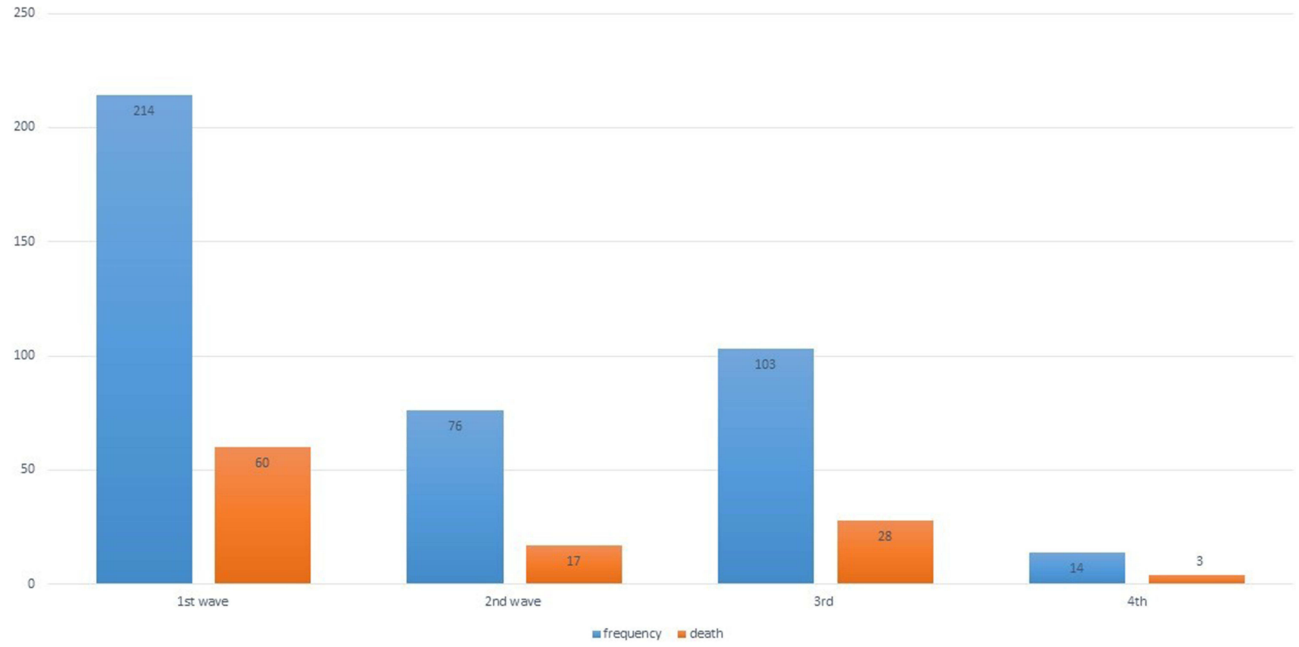

Figure 2 Distribution of admissions and deaths by wave.

Discussion

According to the global mortality, the rate of death was 27%. The mortality affected around a quarter of inpatients. Ngaliema clinic being a tertiary-level hospital, the most severe cases from other COVID-19 treatment centers were transferred there, and 93% of patients who died were already in the severe stage. This mortality was lower than that found in the first wave by Bepouka et al[15] and higher than that found in other DRC facilities[17] and in several African studies.[23–26]

Table 4 Factors Associated with Mortality Among COVID-19 Patients During the 4 Waves in Ngaliema Clinic

Variable	aOR (CI 95%)	P value
Age		
<60 years	1	
≥60 years	2.12(0.69–649)	0.18
Sex		
Female	1	
Male	1.2(0.41–3.59)	0.71
Origin		
Residence	1	
Transferred from centers	0.71 (0.26–1.911)	0.50
Diabetes mellitus		
No	1	
Yes	1.523(0.41–4.38)	0.41
HTN		
No	1	
Yes	1.86(0.62–5.61)	0.26
CRP (mg/l)		
<100	1	
≥100	1.66(0.59–4.68)	0.33

(*Continued*)

Table 4 (Continued).

Variable	aOR (CI 95%)	P value
White blood cells count (cells/mm3)		
<10,000	1	
≥10,000	276(1.25–6.1)	0.01
Severity		
Mild	1	
Moderate	1	
Severe	21.24(1.87–240)	0.01
Use of vitamin C		
No	1	
Yes	0.24(0.08–0.72)	0.01
Use of anticoagulant		
Yes	1	
No	2 0.581(0.15–43.92)	0.51
Use of dexamethason		
Yes	1	
No	0.49(0.04–5.091)	0.55

Abbreviations: HTN, hypertension; CRP, C reactive protein aOR, adjusted odds ratio.

More men died than women (65%). Patients aged 60 or over died more than those under 60. The males and the elderly are particularly vulnerable, with a significant statistical association. This is justified by the fact that the immune system becomes more fragile with age, making this population group vulnerable to COVID-19;[27] as for gender, men were more affected. Two plausible explanations have emerged from the literature. First, in the adaptive immune system, males have a lower T-cell (CD8+, CD4+) and B-cell count as compared to females.[28,29] Second, females have the advantage of the immune regulatory genes located on X chromosome with a higher expression of Toll-like receptor-7 (TLR7).[30,31] Despite the above observations, the multivariate analysis showed no significance for the socio-demographic variables.

Symptoms on admission are dominated by a clinical tetrad of cough, fever, physical asthenia and dyspnoea, whatever the type of wave. These symptoms are the warning signs of the disease. The same symptoms were found in Matangila's study[16] in the first wave and were still predominant in subsequent waves.

With regard to comorbidities, hypertension is the most common comorbidity, accounting for 147 cases, followed by diabetes mellitus, CKD, sickle cell anemia, HIV infection and COPD. The fact that our patients have hypertension, and diabetes mellitus confirms the hypothesis that these patients have ACE2 receptor hyper responsiveness. The latter is the receptor for the COVID-19 virus. Although the majority of patients who died were hypertensive and diabetic, neither of these comorbidities showed any statistically significant difference in the multivariate analysis. This does not include their presence as a factor favoring death. It is already known that hypertension and diabetes mellitus are associated with mortality in COVID-19 patients in Africa.[32,33]

Patients with CKD have increased levels of pro-inflammatory cytokines. The resulting increased oxidative stress drives an inflammatory immune response. An impaired immune system may increase susceptibility to bacterial and viral pulmonary infections.[34,35]

In our study, HIV infection did not have higher mortality than people without HIV. The majority of literature has not supported a higher risk for severe disease among PLWH in Europe and the United States, although a large, population-based study in South Africa reported a higher rate of death due to COVID-19.[36]

As for origin, patients transferred from health centers had a higher rate of death, as approved by the bivariate analysis; as for the multivariate analysis, there was no statistical difference. Nevertheless, the high frequency of death among transferees is justified by the late consultation at the response center, which compromises the prognosis of the disease.

The same finding was made by Bepouka et al.[15] In terms of disease severity, most cases were admitted in a severe state, regardless of the different waves. And our bivariate and multivariate analyses showed a significant statistical difference. The risk of death was 21 times higher in this group of patients than in the others. Most came from other centers that would transfer them, and even those who came from home waited for the situation to worsen before consulting a doctor, due to denial of the disease, especially at the start of the pandemic.

In the light of our observations, we note the precariousness of the patients' biological data. Nevertheless, some of the data submitted to us showed a disturbance in inflammatory biology. After our analyses, we found that death was significantly associated with hyper leukocytosis above 10,000/mm3, with the risk of death multiplied by 2.76. These observations show that COVID-19 disease truly constitutes a septic state and requires proper management. Leukocyte recruitment and production of inflammatory mediators in a positive stimulation cycle.[37–42] The cytokine storm has been reported to play a primary role in the severity of SARS-CoV- 2 infection and lung injury resulting from ARDS, particularly in ICU patients.[43,44]

The therapeutic management of these patients involves a number of therapeutic methods, depending on the severity of the disease. These include oxygen therapy, anticoagulation, dexamethasone. Nevertheless, our analyses showed no significant statistical association apart from the protective effect of vitamin C use. Patients who did not use vitamin C had the highest mortality rate at 67.9%, compared with 32.1% among those who did. This assertion is not strictly confirmed in the literature, the benefit of vitamin C is limited, but some studies show that it benefits could be explained by the fact that vitamin C is an antioxidant that can attenuate the effects of the inflammatory outbreak observed during this pandemic. Vitamin C prevent the production of inflammatory cytokines, lowering pathogen infectivity and virulence, increasing immune defense, minimizing tissue and organ damage, combating oxidative stress. For its protective role against severity and mortality, clinical trials could prove vitamin C's potential role in protecting the population against the current COVID-19 pandemic.[45] The pattern appears to be the same over the 4 waves, with 1st and 3rd waves predominating. This is justified by the fact that control of the disease was precarious in the 1st wave. It declined in the second wave, as the disease became better understood by the population, but rose again in the third wave, probably due to neglect of barrier measures, but with the possibility of the Delta variant emerging, although genomic data are lacking to affirm this.

Limitations and Strengths

Apart from the mono-centric and retrospective nature of the survey, the weaknesses of this study include the absence of biological variables of interest that could contribute to the search for factors associated with death. Another limitation is that the study did not integrate data relating to vaccinated and non-vaccinated patients, as well as different SARS-COV-2 variants. The transformation of continuous variables into categorical ones may reduce granularity. So there are potential information biases because there are potential factors that can influence mortality that we have not necessarily addressed. The study is monocentric, which limits generalizability to other settings within the DRC or sub-Saharan Africa.

Despite these weaknesses, our study is one of the few studies focused on the COVID-19 pandemic, including four waves in the DRC. It has enabled us to identify the factors associated with death and to add to the epidemiological data on an emerging disease.

Conclusion

During the 4 waves at the Ngaliema Clinic, death was often found in elderly, hypertensive and diabetic patients, those with high CRP and hyper leukocytosis. Complaints on admission were most often fever, cough and physical asthenia. Mortality was highest in the 1st wave, followed by the 3rd wave and then the 2nd and 4th waves. Factors associated with mortality were hyper leukocytosis, severe stage and non-use of vitamin C. We recommend that identified risk factors be taken into account to improve early detection and management. There is a need for further research.

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Disclosure

The authors report no competing interests in this work.

References

1. World Health Organization. WHO Coronavirus (COVID-19) Dashboard. Available from: https://covid19.who.int. Accessed January 10, 2023.
2. Sen-crowe B, Sutherland M, Mckenney M, Elkbuli A. A closer look into global hospital beds capacity and resource shortages during the COVID-19 Pandemic. *J Surg Res*. 2020;260:56–63. doi:10.1016/j.jss.2020.11.062
3. Minchella PA, Chanda D, Hines JZ, et al. Clinical characteristics and outcomes of patients hospitalized with COVID-19 during the first 4 waves in Zambia. *JAMA Netw Open*. 2022;5(12):e2246152. PMID: 36512359; PMCID: PMC9856263. doi:10.1001/jamanetworkopen.2022.46152
4. Armstrong RA, Kane AD, Kursumovic E, Oglesby FC, Cook TM. Mortality in patients admitted to intensive care with COVID-19: an updated systematic review and meta-analysis of observational studies. *Anaesthesia*. 2021;76:537–548. doi:10.1111/anae.15425
5. Abobaker A, Alzwi A, Alraied AHA. Overview of the possible role of vitamin C in management of COVID-19. *Pharmacol Rep*. 2020;72 (6):1517–1528. Epub 2020 Oct 28. PMID: 33113146; PMCID: PMC7592143. doi:10.1007/s43440-020-00176-1
6. Sabino EC, Buss LF, Carvalho MPS, et al. Resurgence of COVID-19 in Manaus, Brazil, despite high seroprevalence. *Lancet*. 2021;397 (10273):452–455. doi:10.1016/S0140-6736(21)00183-5
7. Tang JW, Tambyah PA, Hui DS. Emergence of a new SARS-CoV-2 variant in the UK. *J Infect*. 2021;82(4):e27–e28. doi:10.1016/j.jinf.2020.12.024
8. Africa CDC. (2020). COVID-19 situation in Africa: annual report 2020. African Union. Available from: https://africacdc.org/download/africa-cdc-annual-report-2020/. Accessed May 12, 2025.
9. World Health Organization Regional Office for Africa. (2021). Weekly bulletin on COVID-19 in the African region (30 July 2021). WHO. Available from: https://www.afro.who.int/node/12296. Accessed May 12, 2025.
10. Available from: https://www.nicd.ac.za/wp-content/uploads/2022/03/COVID-19-Waves-Comparison_NICD_March2022.pdf. Accessed May 12, 2025.
11. Wolter N, Jassat W, Walaza S, et al. Early assessment of the clinical severity of the SARS-CoV-2 omicron variant in South Africa: a data linkage study. *Lancet*. 2022;399(10323):437–446. Epub 2022 Jan 19. PMID: 35065011; PMCID: PMC8769664. doi:10.1016/S0140-6736(22)00017-4
12. Available from: https://reliefweb.int/report/democratic-republic-congo/last-mile-covid-19-vaccines-drc. Accessed May 12, 2025.
13. Bright B, Babalola CP, Sam-Agudu NA, et al. COVID-19 preparedness: capacity to manufacture vaccines, therapeutics and diagnostics in sub-saharan Africa. *Global Health*. 2021;17:24. doi:10.1186/s12992-021-00668-6
14. Makulo JR, Wumba R, Mandina MN, et al. SARS-CoV2 mutations and impact on mortality: observational study in a sub-saharan Africa hospital. *Virol J*. 2023;20(1):56. PMID: 36998042; PMCID: PMC10062261. doi:10.1186/s12985-023-02014-1
15. Bepouka BI, Mandina M, Makulo JR, et al. Predictors of mortality in COVID-19 patients at Kinshasa UniversityHospital, Democratic Republic of the Congo, from March to June 2020. *Pan Afr Med J*. 2020;37:105. PMID: 33425138; PMCID: PMC7757324. doi:10.11604/pamj.2020.37.105.25279
16. Matangila JR, Nyembu RK, Telo GM, et al. Clinical characteristics of COVID-19 patients hospitalized at Clinique Ngaliema, a public hospital in Kinshasa, in the Democratic Republic of Congo: a retrospective cohort study. *PLoS One*. 2020;15(12):e0244272. PMID: 33338063; PMCID: PMC7748279. doi:10.1371/journal.pone.0244272
17. Nachega JB, Ishoso DK, Otokoye JO, et al. Clinical characteristics and outcomes of patients hospitalized for COVID-19 in Africa: early Insights from the Democratic Republic of the Congo. *Am J Trop Med Hyg*. 2020;103(6):2419–2428. Epub 2020 Oct 2. PMID: 33009770; PMCID: PMC7695108. doi:10.4269/ajtmh.20-1240
18. Nlandu Y, Mafuta D, Sakaji J, et al. Predictors of mortality in COVID-19 patients at Kinshasa Medical Center and a survival analysis: a retrospective cohort study. *BMC Infect Dis*. 2021;21(1):1272. PMID: 34930174; PMCID: PMC8686084. doi:10.1186/s12879-021-06984-x
19. Otshudiema JO, Folefack GLT, Nsio JM, et al. Epidemiological comparison of four COVID-19 waves in the Democratic Republic of the Congo, March 2020-January 2022. *J Epidemiol Glob Health*. 2022;12(3):316–327. Epub 2022 Aug 3. PMID: 35921045; PMCID: PMC9346056. doi:10.1007/s44197-022-00052-6
20. World Health Organization. Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected interim guidance, 13 March 2020. World Health Organization.
21. Hubbard RE, Maier AB, Hilmer SN, et al. Frailty in the face of COVID-19: a systematic review and meta-analysis. *JAMA Netw Open*. 2021;4(6): e2115185. doi:10.1001/jamanetworkopen.2021.15185
22. République Démocratique du Congo. Guide de prise en charge de l´épidémie à COVID-19. *République Démocratique du Congo*. 2020.
23. Abraha HE, Gessesse Z, Gebrecherkos T, et al. Clinical features and risk factors associated with morbidity and mortality among patients with COVID-19 in northern Ethiopia. *Int J Infect Dis*. 2021;105:776–783. Epub 2021 Mar 16. PMID: 33741488; PMCID: PMC7962557. doi:10.1016/j.ijid.2021.03.037
24. Osibogun A, Balogun M, Abayomi A, et al. Outcomes of COVID-19 patients with comorbidities in southwest Nigeria. *PLoS One*. 2021;16(3): e0248281. doi:10.1371/journal.pone.0248281
25. Boulle A, Davies MA, Hussey H, et al. Risk factors for COVID-19 death in a population cohort study from the Western Cape Province, South Africa. *Clin Infect Dis*. 2020:ciaa1198. Epub ahead of print. PMID: 32860699; PMCID: PMC7499501. doi:10.1093/cid/ciaa1198
26. Elimian KO, Ochu CL, Ebhodaghe B, et al. Patient characteristics associated with COVID-19 positivity and fatality in Nigeria: retrospective cohort study. *BMJ Open*. 2020;10(12):e044079. PMID: 33334842; PMCID: PMC7747485. doi:10.1136/bmjopen-2020-044079

27. Chen Y, Klein SL, Garibaldi BT, et al. Aging in COVID-19: vulnerability, immunity and intervention. *Ageing Res Rev*. 2021;65:101205. Epub 2020 Oct 31. PMID: 33137510; PMCID: PMC7604159. doi:10.1016/j.arr.2020.101205
28. Hewagama A, Patel D, Yarlagadda S, Strickland FM, Richardson BC. Stronger inflammatory/cytotoxic T-cell response in women identified by microarray analysis. *Genes Immun*. 2009;10(5):509–516. doi:10.1038/gene.2009.12
29. Abdullah M, Chai P-S, Chong M-Y, et al. Gender effect on in vitro lymphocyte subset levels of healthy individuals. *Cell Immunol*. 2012;272 (2):214–219. doi:10.1016/j.cellimm.2011.10.009
30. Parohan M, Yaghoubi S, Seraji A, Javanbakht MH, Sarraf P, Djalali M. Risk factors for mortality in patients with Coronavirus disease 2019 (COVID-19) infection: a systematic review and meta-analysis of observational studies. *The Aging Male*. 2020;23(5):1416–1424. doi:10.1080/13685538.2020.1774748
31. Dessie ZG, Zewotir T. Mortality-related risk factors of COVID-19: a systematic review and meta-analysis of 42 studies and 423,117 patients. *BMC Infect Dis*. 2021;21(1):855. PMID: 34418980; PMCID: PMC8380115. doi:10.1186/s12879-021-06536-3
32. Bepouka B, Odio O, Mangala D, et al. Diabetes mellitus is associated with higher COVID-19 mortality rates in Sub-Saharan Africa: a systematic review and meta-analysis. *Cureus*. 2022;14(7):e26877. PMID: 35978734; PMCID: PMC9375835. doi:10.7759/cureus.26877
33. Bepouka B, Situakibanza H, Sangare M, et al. Mortality associated with COVID-19 and hypertension in sub-Saharan Africa. A systematic review and meta-analysis. *J Clin Hypertens*. 2022;24(2):99–105. Epub 2022 Jan 27. PMID: 35083847; PMCID: PMC8845466. doi:10.1111/jch.14417
34. Cai R, Zhang J, Zhu Y, Liu L, Liu Y, He Q. Mortality in chronic kidney disease patients with COVID-19: a systematic review and meta-analysis. *Int Urol Nephrol*. 2021;53(8):1623–1629. Epub 2021 Jan 3. PMID: 33389508; PMCID: PMC7778685. doi:10.1007/s11255-020-02740-3
35. Betjes MG. Immune cell dysfunction and inflammation in end-stage renal disease [J]. *Nat Rev Nephrol*. 2013;9(5):255–265. doi:10.1038/nrneph.2013.44
36. Brown LB, Spinelli MA, Gandhi M. The interplay between HIV and COVID-19: summary of the data and responses to date. *Curr Opin HIV AIDS*. 2021;16(1):63–73. PMID: 33186229; PMCID: PMC7735216. doi:10.1097/COH.0000000000000659
37. Farsalinos K, Barbouni A, Niaura R. Systematic review of the prevalence of current smoking among hospitalized COVID-19 patients in China: could nicotine be a therapeutic option? *Intern. Emerg. Med*. 2020;2020:1–8.
38. Wong JP, Viswanathan S, Wang M, et al. Current and future developments in the treatment of virus- induced hypercytokinemia. *Future Med. Chem*. 2017;9(2):169–178. doi:10.4155/fmc-2016-0181
39. Liu Q, Zhou Y-H, Yang Z-Q. The cytokine storm of severe influenza and development of immunomodulatory therapy. *Cellular & Molecular Immunology*. 2016;13(1):3–10. doi:10.1038/cmi.2015.74
40. Tisoncik JR, Korth MJ, Simmons CP, et al. Into the eye of the cytokine storm. *Microbiol. Mol. Biol. Rev*. 2012;76(1):16–32. doi:10.1128/MMBR.05015-11
41. Shimabukuro-Vornhagen A, Gödel P, Subklewe M, et al. Cytokine release syndrome. *Journal for Immunotherapy of Cancer*. 2018;6(1):56. doi:10.1186/s40425-018-0343-9
42. Lee DW, Gardner R, Porter DL, et al. Current concepts in the diagnosis and management of cytokine release syndrome. *Blood*. 2014;124 (2):188–195. doi:10.1182/blood-2014-05-552729
43. Wiersinga WJ, Rhodes A, Cheng AC, et al. Pathophysiology, transmission, diagnosis, and treatment of coronavirus disease 2019 (COVID-19): a review. *JAMA*. 2020;324(8):782–793. doi:10.1001/jama.2020.12839
44. Inandiklioglu N, Akkoc T. Immune responses to SARS-CoV, MERS-CoV and SARS-CoV-2. *Adv. Exp. Med. Biol*. 2020;9:5–12.
45. Mehta N, Pokharna P, Shetty SR. Unwinding the potentials of vitamin C in COVID-19 and other diseases: an updated review. *Nutr Health*. 2023;29 (3):415–433. Epub 2022 Nov 29. PMID: 36445072; PMCID: PMC9713540. doi:10.1177/02601060221139628