

ORIGINAL ARTICLE

Risk factors and clinical features associated with death at the COVID-19 isolation ward of Clairwood Hospital/KwaZulu-Natal, South Africa: A retrospective case-control study.

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Received: 14 September 2025 **Revised:** 10 January 2026 **Accepted:** 18 January 2026 **Available online:** September 2026

DOI: 10.55131/jphd/2026/240314

ABSTRACT

The COVID-19 pandemic posed significant challenges to healthcare systems worldwide. This study aimed to investigate the risk factors associated with death among patients admitted directly to the COVID-19 isolation ward at Clairwood Hospital. A case-control study was undertaken, involving a total of 400 study participants divided equally into 200 cases (deaths) and 200 controls (survivors). Data were collected retrospectively from medical records and analysed using Chi-square tests, univariate, and multivariate logistic regression. The patients had a mean age of 54.1 years (SD=18.9), with 217(54.2%) being female. A respiratory rate exceeding 20 breaths per minute was documented in 177 patients (44.2%), a heart rate greater than 100 beats per minute in 99 patients (24.7%), and a SpO₂ level below 85% on room air in 79 patients (19.7%). Cough was the most common symptom, occurring in 239 (59.7%) patients, while hypertension was the most prevalent comorbidity, present in 157 (39.2%) patients at the time of admission. Chi-square test analyses demonstrated statistically significant associations between mortality and age, fever, cough, shortness of breath, hypertension, diabetes, chronic kidney disease (CKD), obesity, respiratory rate, heart rate, and oxygen saturation (SpO₂) (all $p < 0.05$). On multivariate analysis, increasing age (adjusted odds ratio [aOR]: > 60 years: 12.27 [95% CI: 1.27–118.44]), fever (aOR: 2.86 [95% CI: 1.29–6.31]), shortness of breath (aOR: 9.86 [95% CI: 5.64–17.24]), hypertension (aOR: 2.07 [95% CI: 1.05–4.11]), obesity (aOR: 4.68 [95% CI: 1.43–15.28]), were associated with increased odds of death among COVID-19 patients at admission. No statistically significant associations were observed for other variables after adjustment. Proactive measures to identify and manage these risk factors are crucial in reducing mortality rates and enhancing the overall care of COVID-19 patients in isolation wards.

Keywords:

COVID-19, deaths, risk factors, South Africa.

Citation:

Riziki Ghislain Manimani, Tambwe Willy Muzumbukilwa, Wilbroda Hlolisile Chiya, Benjamin Muthambi, Nombulelo Magula. Risk factors and clinical features associated with death at the COVID-19 isolation ward of Clairwood Hospital/KwaZulu-Natal, South Africa: A retrospective case-control study. J Public Hlth Dev. 2026;24(3): 197-213 (<https://doi.org/10.55131/jphd/2026/240314>)

INTRODUCTION

In December 2019, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-caused coronavirus illness 2019 (COVID-19) first appeared in Hubei Province, China.¹ Subsequently, COVID-19 was not only designated as an international public health emergency but was also declared a worldwide pandemic.¹ As of 8 August 2023, an aggregate of 693,010,830 confirmed COVID-19 cases had been reported worldwide, resulting in 6,905,661 deaths.² Across Africa, there were 12,836,393 documented cases and 258,823 deaths, and specifically in South Africa 4,076,463 cases and 102,595 deaths were reported.² COVID-19 is a multi-system disease with a wide range of clinical symptoms and severity levels depending on host factors such as age, immune response, and comorbidities.^{3, 4} Previous research has identified clinical factors associated with COVID-19 mortality among hospitalized patients in Africa, including advanced age (odds ratio [OR]: 1.04, 95% confidence interval [CI]: 1.02–1.06), male sex (OR: 1.23, 95% CI: 1.07–1.40), hypertension (OR: 1.56, 95% CI: 1.27–1.85), diabetes mellitus (OR: 1.26, 95% CI: 1.01–1.51), chronic kidney disease (OR: 3.39, 95% CI: 2.45–4.71), and critical conditions (OR: 9.04, 95% CI: 3.14–14.94) were among the identified factors.⁵ These findings suggest a convergence of demographic vulnerability and comorbidity burden driving COVID-19 mortality across diverse African settings. Similarly, a study conducted in the Democratic Republic of Congo (DRC) found that ages between 40 and 59 years [adjusted Hazard Ratio (aHR): 4.07; 95% CI: 1.16–8.30], age ≥ 60 years (aHR: 6.65; 95% CI: 1.48–8.88), severe or critical COVID-19 (aHR: 14.05; 95% CI: 6.3–15.67), and the presence of dyspnea (aHR: 5.67; 95% CI: 1.46–21.98) were independently and significantly associated with the risk of death.⁶ Another study conducted in South Africa found that an

elevated D-dimer level was associated with an increased risk of death in the ICU [HR: 1.05; 95% CI: 1.00–1.11].⁷ Clinical presentations of COVID-19 range from mild flu-like symptoms or asymptomatic cases to severe manifestations, including severe pneumonia, acute respiratory distress syndrome, sepsis, thromboembolic events, acute myopericarditis, septic shock, multi-organ failure, and death.^{8, 9} South Africans may face an elevated risk of COVID-19-related mortality, largely attributable to the high burden of both non-communicable and communicable diseases in the population.¹⁰ Despite these studies, there is limited evidence from single-center hospital studies in KwaZulu-Natal, which are important for understanding context-specific clinical and demographic factors that influence mortality. This study aims to address this gap by investigating the risk factors associated with in-hospital deaths at Clairwood Hospital, providing evidence that can guide local clinical management and resource allocation.

METHODS

Study Design

This retrospective case-control study was conducted to evaluate the clinical and demographic factors associated with in-hospital mortality among COVID-19 patients at Clairwood Hospital. Cases were patients who died during hospital admission, and controls were patients who were discharged alive. This design was considered appropriate for evaluating associations between potential risk factors and mortality using routinely collected hospital data. Logistic regression analysis was used to estimate the strength of these associations.

Study Setting

The study was conducted at Clairwood Hospital, a public hospital located at 1 Higginson Highway, Mobeni, KwaZulu-Natal. During the COVID-19

outbreak, the hospital was renovated and designated as a COVID-19 isolation center, receiving all regional COVID-19 patients. All public hospitals in the surrounding region referred confirmed COVID-19 patients requiring isolation or inpatient care to this facility. As a result, the hospital managed a diverse adult patient population with varying disease severity, making it a suitable setting to investigate risk factors for COVID-19-related in-hospital mortality.

Study Period

Medical records of patients admitted between March 2020 and December 2021 were reviewed. This timeframe allowed for the assessment of outcomes across different phases of the epidemic, including periods of high transmission and healthcare system strain.

Study Population

The study population consisted of all COVID-19-positive patients admitted to Clairwood Hospital isolation ward during the study period. A total of 400 patients were included: 200 cases (deaths) and 200 controls (discharged alive), selected at a 1:1 ratio.

Cases were defined as patients with confirmed SARS-CoV-2 infection by polymerase chain reaction (PCR) who died during hospital admission at Clairwood Hospital.

Controls were defined as patients with confirmed SARS-CoV-2 infection by PCR who were admitted during the same period and recovered, being discharged alive from the hospital.

Inclusion and Exclusion Criteria

Inclusion Criteria

Participants were eligible for inclusion if they met all of the following criteria:

- Laboratory-confirmed SARS-CoV-2 infection, established by polymerase chain reaction (PCR);
- Admission to the COVID-19 isolation ward at Clairwood Hospital, KwaZulu-Natal, South Africa;
- Admission during the study period from March 2020 to December 2021;
- Availability of complete medical records documenting admission status, clinical characteristics, and hospital outcome.

Participants meeting the above criteria were classified as follows:

Cases: Patients with confirmed COVID-19 who died during hospital admission.

Controls: Patients with confirmed COVID-19 who recovered and were discharged alive from the hospital.

Exclusion Criteria

Patients were excluded if they met any of the following criteria:

- Unknown or undocumented hospital outcomes (e.g., transfer to another health facility, discharge against medical advice, or loss to follow-up before outcome determination);
- Incomplete or missing medical records that preclude the extraction of key exposure or outcome variables.

Sample size and sampling technique

Relevant data for cases and controls were collected retrospectively from patient medical records at Clairwood Hospital. An indicative sample size and power calculation were performed prior to analysis to assess the adequacy of the proposed sample. With a total sample of 400 patients (200 cases who died during hospital admission and 200 controls discharged alive), assuming a prevalence of a given risk factor of 25–30% among controls, a two-sided α level of 0.05, and

80% power, the study was adequately powered to detect a minimum odds ratio of approximately 1.8–2.0. Cases were identified consecutively from the mortuary register, while controls were selected consecutively from the hospital discharge register within the same study period, using a 1:1 case-to-control ratio to minimize selection bias and ensure comparability.

Data Collection

Data were collected using a standardized, pre-tested data abstraction form specifically developed for this study. Sources of information included admission notes, clinical progress records, laboratory results, and discharge or death summaries. Data abstraction was conducted by trained researchers, with regular cross-checking of a subset of records to ensure completeness and accuracy of the extracted data. Variables collected included demographic characteristics (age and biological sex), pre-existing comorbidities (hypertension, diabetes mellitus, chronic kidney disease, HIV infection, cancer, chronic respiratory disease, tuberculosis, and obesity), presenting symptoms (fever, sore throat, cough, and shortness of breath), and clinical indicators at admission (pulse rate, respiratory rate, and oxygen saturation on room air).

Operational Definitions

COVID-19 diagnosis: Confirmed by a positive real-time polymerase chain reaction (RT-PCR) test for SARS-CoV-2 performed on a respiratory specimen, in accordance with national testing guidelines.

Case (death): A patient with laboratory-confirmed coronavirus disease who succumbed to any cause during the same hospital admission, irrespective of the duration of hospitalization or level of care received.

Control (survivor): A patient with laboratory-confirmed coronavirus infection who recovered clinically and was

discharged alive, with no deaths occurring during the hospital admission.

Obesity was defined as a body mass index ≥ 30 kg/m²

Comorbidities such as hypertension, diabetes, and CKD were ascertained from documented physician diagnoses or prior medical records; patient symptoms and vital signs were recorded from admission notes following standard hospital procedures.

Statistical Analysis

Data were extracted into a standardized Excel database and imported into Stata version 17 (StataCorp, College Station, TX, USA) for statistical analysis. Descriptive statistics were used to summarize study variables, which were expressed as proportions for categorical variables and as means with standard deviations for continuous variables, depending on data distribution. Comparisons between cases and controls were performed using the chi-square or Fisher's exact test for categorical variables and Student's t-test or Wilcoxon rank-sum test for continuous variables, as appropriate.

The association between potential risk factors and COVID-19-related in-hospital mortality was assessed using univariate logistic regression analysis. Variables associated with the outcome at a significance level of $p < 0.05$ in univariate analysis, as well as variables identified a priori based on clinical relevance and evidence from the literature, were included in the multivariable logistic regression model to control for confounding. The final multivariable model was adjusted for age, fever, cough, shortness of breath, hypertension, diabetes mellitus, chronic kidney disease, and obesity. Adjusted odds ratios (aORs) with 95% confidence intervals (CIs) were reported. Multicollinearity among variables was assessed using variance inflation factors (VIF) to ensure model stability.

Missing data were assessed for extent and pattern. A complete-case analysis was conducted, as missingness was minimal for key variables.

Potential sources of bias were considered. Selection bias was minimized by including all eligible cases and controls from the same study period and hospitals. Information bias was reduced through standardized data extraction from medical records, and confounding was addressed through multivariable regression modeling.

Quality control

Data quality assurance procedures included the use of a standardized data abstraction tool, training of data collectors prior to data extraction, and routine consistency and range checks to ensure accuracy and completeness of the dataset before analysis; any discrepancies identified during these checks were

reviewed and resolved through verification against source records.

Ethical Approval

This study was conducted in accordance with the ethical principles of the Declaration of Helsinki. Ethical approval was granted by the University of KwaZulu-Natal Biomedical Research Ethics Committee (UKZN/BREC), under reference number BREC/00005034/2022, with approval issued on 03 April 2023.

Given the retrospective nature of the study and the use of routinely collected hospital medical records, the requirement for informed consent was formally waived by the ethics committee. To ensure patient confidentiality and privacy, no personal identifiers were collected. All data were anonymized prior to analysis, stored on password-protected computers, and accessed only by authorized members of the research team.

RESULTS

Table 1. Demographic Characteristics and symptoms of COVID-19.

Variables	Control Number (%)	Case Number (%)	Total Number (%)	p-value
Demographic characteristics				
Mean (SD) age	45.0(17.4)	63.2(15.8)	54.1(18.9)	
Age group				< 0.001
12-18	9(4.5)	1(0.5)	10(2.5)	
19-40	74(37.0)	24(12.0)	98(24.5)	
41-60	76(38.0)	53(26.5)	129(32.2)	
> 60	41(20.5)	122(61.0)	163(40.7)	
Sex				0.920
Male	92(46.0)	91(45.5)	183(45.7)	
Female	108(54.0)	109(54.5)	217(54.2)	
Symptoms Fever				< 0.001
Yes	15(7.5)	39(19.5)	54(13.5)	
No	185(92.5)	161(80.5)	346(86.5)	

Variables	Control Number (%)	Case Number (%)	Total Number (%)	p-value
Cough				0.006
Yes	106(53.0)	133(66.5)	239(59.7)	
No	94(47.0)	67(33.5)	161(40.3)	
Sore throat				0.889
Yes	30(15.0)	31(15.5)	61(15.2)	
No	170(85.0)	169(84.5)	339(84.7)	
Shortness of breath				< 0.001
Yes	56(28.0)	159(79.5)	215(53.7)	
No	144(72.0)	41(20.5)	185(46.2)	

Table 1 presents the demographic characteristics and presenting symptoms of patients with COVID-19. Cases were significantly older than controls, with a mean age of 63.2 years compared to 45.0 years in the control group. Among cases, 122 patients (61.0%) were aged above 60 years, while only 41 controls (20.5%) fell into this age group. In contrast, younger ages were more common among controls, particularly those aged 19–40 years (74 controls, 37.0%) compared with 24 cases (12.0%). There was no significant difference in sex distribution, with males comprising 91 cases (45.5%) and 92 controls (46.0%).

Regarding symptoms, fever was significantly more common among cases, reported in 39 cases (19.5%) compared to 15 controls (7.5%) ($p < 0.001$). Shortness of breath showed the largest contrast, occurring in 159 cases (79.5%) and 56 controls (28.0%) ($p < 0.001$). Cough was also more frequent among cases, affecting 133 cases (66.5%) versus 106 controls (53.0%) ($p = 0.006$). Sore throat showed no statistically significant difference, occurring in 31 cases (15.5%) and 30 controls (15.0%).

Table 2. Pre-existing comorbidities among patients with coronavirus infection.

Variables	Control Number (%)	Case Number (%)	Total Number (%)	p-value
Comorbidity				< 0.001
Yes	99(49.5)	173(86.5)	272(68.0)	
No	101(50.5)	27(13.5)	128(32.0)	
Hypertension				< 0.001
Yes	46(23.0)	111(55.5)	157(39.2)	
No	154(77.0)	89(44.5)	243(60.7)	
Diabetes				< 0.001
Yes	34(17.0)	68(34.0)	102(25.5)	
No	166(83.0)	132(66.0)	298(74.5)	
CKD				0.006
Yes	3(1.5)	14(7.0)	17(4.2)	
No	197(98.5)	186(93.0)	383(95.7)	

Variables	Control Number (%)	Case Number (%)	Total Number (%)	p-value
HIV				0.163
Yes	44(22.0)	33(16.5)	77(19.2)	
No	156(78.0)	167(83.5)	323(80.7)	
Tuberculosis current				0.312
Yes	3(1.5)	6(3.0)	9(2.2)	
No	197(98.5)	194(97.0)	391(97.7)	
Tuberculosis previous				0.126
Yes	5(2.5)	11(5.5)	16(4.0)	
No	195(97.5)	189(94.5)	384(96.0)	
Asthma				0.207
Yes	9(4.5)	15(7.5)	24(6.0)	
No	191(95.5)	185(92.5)	376(94.0)	
Obesity				< 0.001
Yes	5(2.5)	23(11.5)	28(7.0)	
No	195(97.5)	177(88.5)	372(93.0)	
Mental health disorder				0.359
Yes	7(3.5)	4(2.0)	11(2.75)	
No	193(96.5)	196(98.0)	389(97.2)	
Cancer				0.177
Yes	1(0.5)	4(2.0)	5(1.2)	
No	199(99.5)	196(98.0)	395(98.7)	

Table 2 summarizes the distribution of pre-existing comorbidities among COVID-19 patients. Overall comorbidity was significantly more common among cases than controls (86.5% vs. 49.5%, $p < 0.001$). Hypertension and diabetes were also markedly higher in cases, with 55.5% and 34.0% affected, compared with 23.0% and 17.0% in controls, respectively (both $p < 0.001$). Chronic kidney disease was present in 7.0% of cases versus 1.5% of controls ($p = 0.006$). Obesity was likewise

more frequently observed among cases (11.5%) than controls (2.5%) ($p < 0.001$). In contrast, no significant differences were found between cases and controls regarding HIV infection, current or previous tuberculosis, asthma, mental health disorders, or cancer (all $p > 0.05$). These findings indicate that several metabolic and chronic conditions were disproportionately associated with COVID-19 cases in this study.

Table 3. CD4 and VL for HIV-COVID-19 patients

	Control Number (%)	Case Number (%)	Total Number (%)	p-value
CD4(cells/mm³)				< 0.001
<200	7(3.5)	18(9.0)	25(6.2)	
200-500	15(7.5)	5(2.5)	20(5.0)	
>500	12(6.0)	----	12(3.0)	
Missing results	10(5.0)	10(5.0)	20(5.0)	
HIV-unknown	156(78)	167(83.5)	323(80.75)	
Viral load (copies/ml)				0.074
<50	25(12.5)	11(5.5)	36(9.0)	
50-200	----	3(1.5)	3(0.7)	
1001-100,000	1(0.5)	3(1.5)	4(1.0)	
>100,000	3(1.5)	2(1.0)	5(1.2)	
Missing	15(7.5)	14(7.0)	29(7.2)	
Unknown HIV	156(78.0)	167(83.5)	323(80.7)	

Table 3 presents the distribution of CD4 counts and HIV viral load among HIV–COVID-19 patients. CD4 levels differed significantly between the two groups ($p < 0.001$). A higher proportion of cases had CD4 counts <200 cells/mm³ (9.0%) compared with controls (3.5%), while CD4 levels of 200–500 cells/mm³ were more common among controls (7.5%) than cases (2.5%). Only controls had CD4 counts >500 cells/mm³. A large proportion of both groups had unknown CD4 results.

In contrast, viral load distribution did not differ significantly between cases and controls ($p = 0.074$). Most patients in both groups had undetectable or low viral load (<50 copies/mL), and the number of individuals with higher viral load categories was small. These findings indicate that lower CD4 levels were more frequently observed among cases, whereas viral load patterns were comparable between the two groups.

Table 4. Vital signs of COVID-19 patients at hospital admission

Variables	Control Number (%)	Case Number (%)	Total Number (%)	p-value
Temperature (°C)				0.056
<37	182(91.0)	183(91.5)	365(91.2)	
37-38	16(8.0)	12(6.0)	28(7.0)	
>38	----	5(2.5)	5(1.2)	
Missing	2(1.0)	-----	2(0.5)	

Variables	Control Number (%)	Case Number (%)	Total Number (%)	p-value
Respiratory rate (RR/min)				< 0.001
12-20	162(81.0)	59(29.5)	221(55.2)	
>20	38(19.0)	140(70.0)	177(44.2)	
Missing	-----	1(0.5)	1(0.2)	
Heart rate (Beats/min)				< 0.001
<60	2(1.0)	2(1.0)	4(1.0)	
60-100	166(83.0)	131(65.5)	297(74.2)	
>100	32(16.0)	67(33.5)	99(24.7)	
SpO₂ (%) on RA				< 0.001
95–100	143(71.5)	17(8.5)	160(40.0)	
91–94	24(12.0)	15(7.5)	39(9.7)	
86–90	6(3.0)	30(15.0)	36(9.0)	
<85	8(4.0)	71(35.5)	79(19.7)	
Missing	19(9.5)	67(33.5)	86(21.5)	

Abbreviations: RA: room air, SpO₂: oxygen saturation.

Table 4 describes the vital signs of COVID-19 patients at hospital admission. Temperature distributions were similar between the two groups, with most patients presenting with temperatures below 37 °C (91.0% of controls and 91.5% of cases), and no statistically significant difference was observed. Respiratory rate showed a marked contrast: tachypnea (>20 breaths/min) was present in 140 cases (70.0%) compared with 38 controls (19.0%) ($p < 0.001$), indicating substantially worse respiratory compromise among cases. Heart rate also differed

significantly, with tachycardia (>100 beats/min) observed in 67 cases (33.5%) versus 32 controls (16.0%) ($p < 0.001$). Oxygen saturation showed the most pronounced disparity. Only 17 cases (8.5%) had normal SpO₂ (95–100%) on room air, compared with 143 controls (71.5%). Severe hypoxia (SpO₂ <85%) was recorded in 71 cases (35.5%) compared with 8 controls (4.0%) ($p < 0.001$). Missing SpO₂ data were notably higher among cases (33.5%) than controls (9.5%), which may reflect documentation gaps or severe presentations.

Table 5. Association between demographic characteristics, symptoms at admission, pre-existing comorbidities, and in hospital mortality among patients with coronavirus infection at Clairwood Hospital

Variables	OR (95% CI)	p-value	aOR (95% CI)	p-value
Age group (years)				
12-18	Ref		Ref	
19-40	2.91(0.35-24.23)	0.321	1.67(0.17-16.12)	0.653
41-60	6.27(0.77-51.02)	0.086	2.49(0.26-23.63)	0.426
> 60	26.78(3.29-217.83)	0.002	12.27(1.27-118.44)	0.030

Variables	OR (95% CI)	p-value	aOR (95% CI)	p-value
Sex				
Female	Ref			
Male	0.98(0.66-1.45)	0.920	NA*	NA*
Symptoms at admission				
Fever	2.98(1.58-5.61)	0.001	2.86(1.29-6.31)	0.009
Cough	1.76(1.17-2.63)	0.006	1.19(0.69-2.07)	0.520
Sore throat	1.03(0.60-1.79)	0.889	NA*	NA*
Shortness of breath	9.97(6.28-15.82)	< 0.001	9.86(5.64-17.24)	< 0.001
Pre-existing comorbidity				
Hypertension	4.17(2.71-6.42)	< 0.001	2.07(1.05-4.11)	0.036
Diabetes	2.51(1.57-4.02)	< 0.001	0.68(0.33-1.38)	0.293
CKD	4.94(1.39-17.47)	0.013	1.56(0.38-6.28)	0.530
Asthma	1.72(0.73-4.02)	0.211	NA*	NA*
Tuberculosis current	2.03(0.50-8.23)	0.321	NA*	NA*
Obesity	5.06(1.88-13.61)	0.001	4.68(1.43-15.28)	0.011
Mental health disorder	0.56(0.16-1.95)	0.365	NA*	NA*
Cancer	4.06(0.44-36.65)	0.212	NA*	NA*

Abbreviations: aOR: adjusted odds ratio, CI: confidence interval, CKD: chronic kidney disease, HIV: human immunodeficiency virus,*NA: not applicable, indicate variables for which multivariate analysis could not be conducted because these variables were not statistically significant in the univariate analysis OR: odds ratio.

Table 5 presents the association between demographic characteristics, symptoms at admission, pre-existing comorbidities, and mortality among COVID-19 patients at Clairwood Hospital. Age showed a strong association with death. Compared with the 12–18-year reference group, patients aged >60 years had significantly higher odds of mortality in both unadjusted (OR = 26.78; 95% CI: 3.29–217.83; $p = 0.002$) and adjusted analyses (aOR = 12.27; 95% CI: 1.27–118.44; $p = 0.030$). The 19–40 and 41–60 age groups showed increased odds in the unadjusted analysis, but these associations were not statistically significant after adjustment. Sex was not associated with mortality. Regarding clinical symptoms, fever and shortness of breath were significantly associated with death in both unadjusted and adjusted models. Shortness of breath demonstrated the strongest association (aOR = 9.86; 95% CI: 5.64–17.24; $p < 0.001$). Cough was significant in the unadjusted model but lost significance after adjustment, while sore throat showed

no association. Among pre-existing comorbidities, hypertension and obesity remained significant predictors of mortality after adjustment. Hypertensive patients had twice the odds of death (aOR = 2.07; 95% CI: 1.05–4.11; $p = 0.036$), and obese patients had nearly five times higher odds (aOR = 4.68; 95% CI: 1.43–15.28; $p = 0.011$). Diabetes and chronic kidney disease were significant only in unadjusted analyses and lost significance in adjusted models. Other comorbidities including asthma, tuberculosis, mental health disorders, and cancer did not show significant associations with mortality.

DISCUSSION

In this study, we found that increasing age (>60 years), fever, shortness of breath, hypertension, and obesity were significantly associated with mortality among COVID-19 patients admitted to Clairwood Hospital. To enhance clarity, we first discuss demographic predictors,

followed by clinical presentation, and finally comorbid conditions.

Consistent with our results, numerous previous studies have demonstrated a significant relationship between advancing age and mortality among patients with laboratory-confirmed coronavirus disease.^{6,11,12} Older age increases mortality primarily because of cumulative, age-related alterations in immune function and physiology that reduce the ability to effectively control viral infections and tolerate systemic inflammation. This association is likely attributable to age-related biological changes in the immune system that increase susceptibility to infectious diseases and chronic comorbid conditions, thereby adversely affecting disease progression and clinical outcomes.¹³ Aging is associated with functional alterations in both adaptive immune cells, including CD4⁺ and CD8⁺ T lymphocytes, as well as B cells, resulting in diminished immune responsiveness.¹⁴ Immunosenescence—the progressive remodeling and decline of immune function with advancing age—together with an increased risk of immunopathology due to reduced B- and T-cell activity, is thought to play a central role in the heightened vulnerability of older individuals to severe COVID-19 and mortality.¹⁵ Age-related impairments in both innate and adaptive immunity compromise the type I interferon (IFN) response, a key antiviral defense mechanism. This impairment is further exacerbated by SARS-CoV-2 non-structural proteins, which suppress IFN signaling and weaken CD8⁺ T-cell-mediated viral clearance.¹⁷ In addition, older adults exhibit reduced de novo T-cell responses and often harbor underlying conditions, including persistent viral infections such as cytomegalovirus (CMV), which may further increase susceptibility to severe COVID-19.¹⁵ Although the precise mechanisms remain incompletely

understood, studies have shown that older convalescent plasma donors develop higher titers of SARS-CoV-2-specific IgG and neutralizing antibodies compared with younger individuals, suggesting qualitative differences in immune responses across age groups.^{9,15,16} Furthermore, ageing is associated with a chronic low-grade inflammatory phenotype, which may be exacerbated by factors including smoking, reduced sex steroid secretion, and increased adiposity. Collectively, these factors contribute to a dysregulated pro-inflammatory environment that promotes heightened cytokine production and intensifies host immune activation following COVID-19.^{15,18} This inflammatory imbalance may also influence angiotensin-converting enzyme 2 (ACE2) expression and viral entry.^{15,18} Additionally, increased production of type 2 cytokines can impair effective viral control, prolong inflammatory responses, and contribute to disease severity and fatal outcomes. Elevated angiotensin-converting enzyme activity within cardiac and pulmonary tissues has also been suggested as a potential contributor to the heightened mortality risk observed among older adults with COVID-19.^{19,20,21,22} The effect estimates for age should be interpreted cautiously due to the wide confidence intervals, which suggest variability in the data.

Beyond demographic factors, we next examined presenting symptoms that reflect disease severity at admission. Fever at admission emerged as an independent predictor of mortality in our study. Fever increases mortality risk in COVID-19 because it often reflects an exaggerated and dysregulated inflammatory response rather than an effective, protective immune reaction, particularly in vulnerable populations. Fever represents activation of the host immune response and is commonly associated with higher viral load, systemic

inflammation, and disease severity in COVID-19.³⁴ Several studies have reported that persistent or high-grade fever is associated with severe disease progression and poor outcomes, particularly when accompanied by respiratory symptoms.^{6,11} In older adults and patients with comorbidities, fever may paradoxically signal immune dysregulation rather than effective viral clearance, as the inflammatory response may become excessive and maladaptive.³³ Sustained fever contributes to increased metabolic demand, endothelial activation, and cytokine release, thereby exacerbating hypoxia, coagulopathy, and organ dysfunction.³² In this context, fever may act as a clinical marker of hyperinflammation and impending clinical deterioration, rather than a protective host response.

Similarly, respiratory symptoms were strong predictors of adverse outcomes. Our findings demonstrate that shortness of breath at admission was independently associated with increased mortality among patients with COVID-19, in line with previously reported studies.^{6,11,23} Dyspnea is widely recognized as a clinical marker of advanced pulmonary involvement and disease severity, reflecting impaired gas exchange, extensive lung parenchymal damage, and progression toward acute respiratory distress syndrome (ARDS). The presence of shortness of breath, particularly when accompanied by fever, has also been associated with a heightened risk of COVID-19–related coagulopathy and thromboembolic complications, including pulmonary embolism. This observation is consistent with reports from European cohorts that documented a high incidence of pulmonary embolism among hospitalized COVID-19 patients, especially those presenting with respiratory distress.²⁴ The hyperinflammatory state induced by SARS-CoV-2 infection promotes endothelial injury, platelet activation, and dysregulation of the coagulation cascade,

thereby increasing thrombotic risk and contributing to adverse clinical outcomes.²⁵ Furthermore, dyspnea reflects reduced pulmonary reserve and compromised respiratory mechanics, which limit the patient's ability to tolerate the physiological stress imposed by severe viral infection. Individuals presenting with shortness of breath often have diminished lung capacity and impaired oxygenation, rendering them less capable of mounting effective compensatory responses during acute illness.²⁵ In the context of COVID-19, this reduced functional reserve is strongly associated with rapid clinical deterioration and poor prognosis. Collectively, these findings underscore the prognostic importance of shortness of breath as an early clinical indicator of severe disease and mortality risk in COVID-19 patients, highlighting the need for prompt recognition and aggressive clinical management in patients presenting with respiratory symptoms.

Finally, we evaluated the role of chronic comorbid conditions in modifying mortality risk. Our findings indicate that hypertension was independently associated with increased mortality among patients with COVID-19. This observation is consistent with several meta-analyses and large cohort studies that have identified hypertension as a significant risk factor for adverse COVID-19 outcomes.^{5,14,19} However, our results contrast with other reports that did not observe a significant association between hypertension and mortality.^{26,27} The heterogeneous findings in the literature may reflect differences in study populations, adjustment for confounders, and definitions of disease severity. Mechanistically, severe COVID-19 outcomes in patients with hypertension have been attributed to endothelial dysfunction and dysregulation of the renin–angiotensin system (RAS). Hypertension is associated with a sustained pro-inflammatory and pro-oxidative state, characterized by elevated angiotensin II

(Ang II) levels, alongside increased concentrations of chemokines and inflammatory cytokines, including interleukin-6 (IL-6) and tumor necrosis factor (TNF).^{28,29} During infection with the novel coronavirus, activation of the classical RAS pathway (ACE/Ang II/AT1R) along with suppression of the counter-regulatory ACE2/Ang-(1-7)/Mas axis has been associated with adverse clinical outcomes.^{29,30} This dysregulation promotes vasoconstriction, inflammation, endothelial damage, and thrombogenesis, collectively contributing to worsened clinical outcomes and increased mortality in hypertensive patients with coronavirus infection.³⁰

In addition, obesity emerged as a significant predictor of mortality in our study population, in line with previous studies reporting a relationship between obesity and heightened disease progression and mortality in patients with COVID-19.³¹ Obesity is associated with profound immune and metabolic dysregulation, including altered regulatory T-cell function within adipose tissue and a skewing of immune responses toward the pro-inflammatory TH17 T-cell sub-lineage.³¹ These immunological alterations are accompanied by elevated circulating levels of inflammatory mediators such as IL-6, IL-23/IL-17, TNF- α , transforming growth factor (TGF), macrophage migration inhibitory factor, and macrophage inflammatory protein-1 α .¹⁴ Furthermore, obesity adversely affects respiratory physiology, leading to reduced lung compliance, impaired ventilatory mechanics, and decreased functional respiratory reserve, which may exacerbate hypoxemia during acute viral infections.¹⁴ Obesity is also associated with a heightened pro-thrombotic and pro-inflammatory state, factors that have been implicated in poor outcomes in severe viral pneumonias, including H1N1 influenza.¹⁴ Importantly,

obesity extends beyond excess subcutaneous fat and includes the accumulation of visceral, epicardial, and perivascular adipose tissue. This ectopic fat distribution contributes to chronic systemic inflammation, endothelial dysfunction, and a vasoconstrictive milieu, thereby increasing the risk of insulin resistance, type 2 diabetes, hypertension, cardiovascular disease, and impaired immune responses.³¹ Visceral obesity, in particular, has been associated with increased mortality among critically ill patients with acute respiratory distress syndrome and other chronic illnesses, further supporting its role as a key determinant of adverse COVID-19 outcomes.³¹

STUDY LIMITATIONS

Despite the strengths of this study, several limitations should be acknowledged. First, the retrospective and hospital-based design introduces the possibility of selection bias, as the analysis included only patients who were admitted to Clairwood Hospital and may therefore overrepresent more severe cases of COVID-19. Second, missing data for some clinical variables, particularly oxygen saturation (SpO₂), may have limited the precision of certain estimates and reduced the ability to fully adjust for disease severity at presentation. Third, as this was a single-center study, the findings may reflect local patient characteristics, healthcare practices, and admission criteria, which may limit the generalizability of the results to other settings or populations. Fourth, although multivariable analysis was performed, residual confounding cannot be excluded, as some potentially important factors—such as socioeconomic status, treatment variations, vaccination status, timing of presentation, and specific laboratory biomarkers—were not measured

or available for inclusion in the models. Finally, the observational nature of the study precludes causal inference, and the associations identified should be interpreted as correlational rather than causal. Future multicenter prospective studies with more comprehensive data collection are warranted to validate these findings and enhance their external applicability.

CONCLUSION

In this study, we identified key factors independently associated with mortality among COVID-19 patients admitted directly to the isolation ward at Clairwood Hospital. Increasing age (>60 years), fever at admission, shortness of breath, hypertension, and obesity were significantly associated with higher odds of death, while other clinical and demographic factors did not remain significant after multivariate adjustment. These findings provide evidence of the specific patient characteristics and presenting features most strongly linked to adverse outcomes during hospitalization for COVID-19. By focusing strictly on the observed associations, this study provides a clearer understanding of the clinical determinants of in-hospital mortality, which can inform targeted management strategies in resource-limited settings to improve patient outcomes.

RECOMMENDATION

Based on the study findings, mortality among COVID-19 patients admitted to Clairwood Hospital was significantly associated with increasing age (>60 years), fever, shortness of breath, hypertension, and obesity. Clinical care should prioritize early identification and close monitoring of patients with these risk factors. Specifically, elderly patients and those presenting with shortness of breath, hypertension, or obesity require enhanced

clinical observation and timely intervention.

Public health measures should focus on risk stratification at admission to ensure high-risk patients are prioritized for supportive care, oxygen therapy, and monitoring of vital signs, particularly respiratory function and oxygen saturation. Research implications include further investigation into targeted interventions for high-risk groups to reduce mortality, and prospective studies to validate predictive risk models for COVID-19 outcomes in similar hospital settings.

AUTHOR CONTRIBUTIONS

RGM: Conceptualization, Methodology, Data Collection, Data Curation, Formal Analysis, and Writing – Original Draft. TWM: Data Collection, Resources, Validation, Writing – Review & Editing. WHC: Formal Analysis, Visualization, Writing – Review & Editing. BM: Investigation, Data Curation, Writing Review & Editing. NM: Conceptualization, Supervision, Writing – Review & Editing.

ETHICAL CONSIDERATION

This study received ethical approval from the University of KwaZulu-Natal Biomedical Research Ethics Committee (UKZN/BREC). The approved protocol number is BREC/00005034/2022, with the approval granted on 03 April 2023.

ACKNOWLEDGEMENTS

The authors express their profound appreciation to the Nelson R. Mandela School of Medicine at the University of KwaZulu-Natal.

CONFLICT OF INTEREST

All authors declare no conflict of interest.

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