


# Clinical manifestations and treatment outcomes among hospitalised COVID-19 patients in tertiary hospitals in Tanzania, 2021–2022: a retrospective cohort study

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## ABSTRACT

**Background** There have been differential mortality rates from COVID-19 in different parts of the world. It is not clear whether the clinical presentation does also differ, thus the need for this study in a sub-Saharan African setting. The aim of this study was to describe the clinical manifestations and outcomes of patients diagnosed with COVID-19 in selected tertiary hospitals in Tanzania.

**Methods** This was a retrospective analysis of hospitalised adults confirmed SAR-COV-2 infection in five tertiary-level hospitals in Tanzania. Data collected and analysed included sociodemographic, radiological and clinical characteristics of the patients as well as the outcome of the admission (discharge vs death).

**Results** Out of 1387 COVID-19 patients, 52% were males. The median age was 60 years (IQR)=(19–102)). The most common symptoms were dyspnoea (943, 68%), cough (889, 64%), fever (597, 43%) and fatigue (570, 41%). In-hospital mortality was (476, 34%). Mortality significantly increased with increasing age, being the most in age >90 years (aHR (95% CI)=4.4 (2.52 to 28.82), p=0.02). Other predictors of mortality were not possessing a health insurance, (aHR (95% CI)=3.7 (1.09 to 14.25), p=0.04); chest pain, (aHR (95% CI)=2.27 (1.36 to 4.13), p=0.03); HIV positivity, (aHR (95% CI)=3.9 (1.46 to 8.15), p=0.03); neutrophilia, (aHR (95% CI)=1.12 (1.01 to 2.65), p=0.03); no use of ivermectin, (aHR (95% CI)=1.21 (1.04 to 1.57), p=0.04) and non-use of steroids, (aHR (95% CI)=1.36 (1.18 to 2.78), p=0.04). The retrospective nature of this study which based on documented patients' records, with a large number of patients left out of the analysis due to missed data, this might in a way affect the results of the present study.

**Conclusion** In-hospital mortality was 34%. The independent predictors of mortality were advanced age, HIV infection, no possession of a health insurance, chest pain, neutrophilia and no use of steroids or ivermectin.

## WHAT IS ALREADY KNOWN ON THIS TOPIC

- ⇒ COVID-19 caused more deaths in Americas, Europe and Asia than it did in Africa.
- ⇒ The most affected patients were predominantly male, aged 60 years or older and having comorbidities such as diabetes mellitus and hypertension.

## WHAT THIS STUDY ADDS

- ⇒ COVID-19 presents more or less the same in an African country, Tanzania as it is in other parts of the world.
- ⇒ HIV infection but not diabetes mellitus nor hypertension predicted mortality in Tanzania, suggesting a possibility of differential mortality as there are more non-communicable diseases patients than HIV-infected patients worldwide

## HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

- ⇒ Health authorities need to conduct customised research on the predictors and preventive strategies for COVID-19 mortality.
- ⇒ Healthcare practitioners need to actively assess the factors that influence mortality among COVID-19 patients including HIV infection and manage them appropriately to reduce COVID-19-associated mortality.

## INTRODUCTION

By March 2023, a total of 760 million infections from SARS-COV-2 and about 6.9 million deaths had been recorded globally,<sup>1</sup> making COVID-19 the number one killer from a single infectious cause, surpassing tuberculosis.<sup>2</sup>

Compared with the Americas, Europe and Asia, African countries including Tanzania have recorded low incidence of symptomatic COVID-19 infection as well as mortality due to yet unexplained reasons. Nevertheless, the COVID-19 pandemic has added to the disease burden in sub-Saharan Africa, which also has the highest numbers of other infectious diseases and escalating rates of non-communicable diseases.<sup>3</sup>

Although COVID-19 is primarily a respiratory disease, studies suggest that it can lead to cardiovascular,<sup>4-7</sup> haematological,<sup>4 8</sup> hepatic,<sup>4</sup> neurological,<sup>5 9</sup> renal<sup>4 10</sup> and other complications.<sup>4</sup> Fever, cough and fatigue are the most common presentations, seen in 60%–87%, 72%–85% and 20%–36% of the patients with COVID-19, respectively.<sup>5 11-15</sup> Dyspnoea and chest pain are the most frightening symptoms and are seen in about a quarter of the patients.<sup>14 15</sup> Neurological symptoms include headache in about 34%<sup>5 16 17</sup> and impaired sense of smell and taste in 7% of patients.<sup>16</sup> Other symptoms reported in acute COVID-19 included but were not limited to muscle and pain in up to 34%, nausea (4.1%), anorexia (2.6%), sore throat (1.6%)<sup>11 13 15</sup> diarrhoea, vomiting and abdominal pain.<sup>5 9</sup>

Hypoxaemia has been strongly associated with worsening of clinical outcomes. Xie *et al* in a study done in 2020 in Wuhan China found that oxygen saturation (SpO<sub>2</sub>) of less than 90.5% at admission was related to an almost threefold increased risk of dying.<sup>18</sup>

The pulmonary abnormalities seen in the chest imaging have been commonly bilateral peripheral ground glass opacities (GGO). Consolidation developed later in the course of COVID-19 illness.<sup>19</sup> An earlier imaging study in Wuhan, China reported that bilateral lung abnormalities were the predominant findings in 79% of patients followed by peripheral abnormalities, (54%). GGO was found in 65% of the patients and mainly involved the right lower lobes (27%).<sup>19</sup>

Leucopenia and lymphopenia are the most common laboratory findings found in patients with COVID-19,<sup>4</sup> though they are non-specific. Other abnormal laboratory findings include elevated levels of lactate dehydrogenase (LDH), C reactive protein (CRP), aminotransferase, D-dimers and ferritin.<sup>4 5</sup> Patients with elevated levels of D-dimer were found to have a threefold risk of mortality among COVID-19 patients in a study done in India.<sup>5 20</sup>

Several factors have been associated with adverse outcomes and mortality among COVID-19 patients. These include male sex, age of more than 55 years,<sup>21 22</sup> pre-existing comorbidities,<sup>21 23 24</sup> hypoxic state at admission, radiological abnormalities,<sup>25</sup> abnormal laboratory results<sup>26</sup> and biomarkers of multiple organ failures.<sup>27</sup> The presence of these factors has been used by physicians to predict the severity of COVID-19 and the risk of death.<sup>26</sup>

Previous studies of COVID-19 patients reported that patients who were 60 years or older or were male or presented with low SpO<sub>2</sub> levels at the time of admission were more likely to die of COVID-19.<sup>28-30</sup> Lower socioeconomic status was also associated with increased risk of

death from COVID-19.<sup>28 31</sup> Some studies conducted early during the pandemic reported more severe COVID-19 for smokers.<sup>32 33</sup> Of note, these studies did not consider the important confounding factors like age, sex and pre-existing comorbidities.<sup>32 33</sup>

The most common comorbidities reported in previous studies include hypertension (affecting 7.7% of the COVID-19 patients), diabetes mellitus (DM) (4.6%), cardiovascular diseases (2.6%), asthma (1.6%) and other comorbidities (2.6%).<sup>15 29 30</sup> The Centers for Disease Control and Prevention (CDC) has included sickle cell disease, asthma and pregnancy as risk factors for severe COVID-19.<sup>34</sup>

Treatment of SARS-CoV-2 infection relied mostly on symptomatic treatment and supportive care of the presenting problems.<sup>35</sup> Management strategies are directed to address inflammation, hypercoagulability, oxygenation, vitamin and supplements, restoration and maintenance of hydration, prophylactic antibiotics and promising antivirals.<sup>35</sup> Administration of systemic steroids in patients with severe COVID-19 has shown to reduce the risk of mortality by 64%.<sup>36</sup> Among antivirals, remdesivir has been shown to lower the risk of mortality, accelerate patients' recovery and reduce progression to invasive ventilation, compared with best supportive care among hospitalised COVID-19 patients requiring any or low supplemental oxygen at baseline.<sup>37</sup> Invasive ventilation has been associated with 36% of mortality in the ICU among severe COVID-19 patients.<sup>22</sup> Ivermectin was reported by Caly *et al* to inhibit SARS-CoV-2 in vitro and has been used during acute COVID-19.<sup>38</sup> COVID-19 vaccines have been reported to reduce the severity and transmissibility of SARS-CoV-2 infection.<sup>12 39</sup>

Our knowledge of clinical description, risk factors and treatment outcomes of COVID-19 in Tanzania is limited to reports from other countries, despite the results of only a single centred small study done in Tanzania<sup>30</sup> and in Kinshasa Democratic Republic of the Congo (DRC).<sup>29</sup> This study, therefore, aimed at describing clinical manifestations and treatment outcomes of patients diagnosed and hospitalised with SARS-CoV-2 in a Tanzanian population.

## MATERIALS AND METHODS

### Design and setting of the study

This was a retrospective analysis of archived data of COVID-19 patients in five tertiary hospitals in Tanzania, namely Muhimbili National Hospital (MNH) Upanga and Mloganzila campuses in Dar es Salaam city representing the coastal zone, Kilimanjaro Christian Medical Center (KCMC) in Kilimanjaro representing the northern zone, Bugando Medical Center (BMC) in Mwanza representing the lake zone, Benjamin Mkapa Hospital (BMH) in Dodoma representing the central zone and Mbeya Zonal Referral Hospital (MZRH) in Mbeya representing the southern highlands zone. The hospitals were selected conveniently due to their capacity to accommodate and

manage severe respiratory diseases including COVID-19. Management of COVID-19 in all five hospitals in Tanzania followed the COVID-19 treatment guideline of Tanzania of 2021.<sup>35</sup> COVID-19 vaccines were not readily available in Tanzania till September 2021. We studied archived data of patients aged 18 years or older who were admitted to the participating hospitals from 26 March 2021 to 30 July 2022 with COVID-19 confirmed by PCR test. PCR tests/reagents were not always available in the country before March 2021, thus, patients seen in those hospitals during that time were not part of this study. Patients who have incomplete data of more than 10% were excluded from the analysis.

### Data collection procedures

Data were collected for the period of 6 months from November 2022 to May 2023. We searched patients' data from hospitals' record departments to identify patients who were hospitalised with the diagnosis of either confirmed or suspected COVID-19 disease or other diagnoses which in our experience were often used instead of COVID-19. We obtained file numbers of these patients from the records departments and used them to search for COVID-19 PCR results from the hospitals' records and/or from the National Public Health Laboratory. Only data of patients with positive PCR tests were considered for this study. File numbers were also used to obtain both hard copy files and electronic data of the patients. Electronic clinical research forms created in Research Electronic Data Capture (REDCap) software<sup>40</sup> were used to document patients' data from both hard copy files and electronic databases. Patients' names and registration numbers were not entered in a database. Patients were assigned a special study number which was entered in the database. The database was only accessed by the study team with special passwords. The information collected included sociodemographic data and vital signs (respiratory rate, oxygen saturation and heart rate), symptoms (respiratory, cardiovascular, gastrointestinal and central nervous system), duration of hospital admission and comorbidities. We also recorded inflammatory markers (serum ferritin, LDH, CRP and erythrocyte sedimentation rate), complete blood count, D-dimer, cardiac troponin, renal function test, liver enzymes, fasting blood glucose (FBG), CD4 and viral load (VL) both at admission. We also documented treatment modalities and mortality.

### Statistical analysis

With our sample size of 1387, there is 80% power to detect a risk factor with a prevalence of 0.06 if it has an HR of at least 1.4. Study data were collected and managed using REDCap software hosted at MUHAS.<sup>40</sup> Analysis was done by using STATA V.17. Sociodemographic, clinical and radiological characteristics of the patients were categorised, presented as frequencies and proportions and compared using  $\chi^2$  test or Fisher's exact test. We used Fisher's exact test for variables with less than 25 responses, that is, variables with low diversity (eg, binary

variables with a prevalence of under 2% of one category). All the variables were not normally distributed; hence, we used median and IQR to present continuous variables and compared by Wilcoxon rank sum test. Cox regression analysis was used to assess the relationship between sociodemographic factors, clinical presentations, comorbidities, and treatment modalities and COVID-19 outcomes. Covariates for the multivariate cox regression were selected using a p value threshold of 0.05 from the univariate analysis. Some potential risk factors that have been widely reported in the literature were forced into the multivariate model. For example, sex and dyspnoea had a p value greater than 0.05, it was entered into the multivariate model due to its clinical significance. Variables with low diversity (eg, binary variables with a prevalence of under 2% of one category) and variables with large numbers of missing data were not included in the model, regardless of their meeting other criteria. A  $p < 0.05$  was considered significant in all analyses.

### Patient and public involvement

This was a retrospective study; hence patients were not involved directly, but permissions to use patients' data were obtained from the heads of participating hospitals.

## RESULTS

A total of 10237 suspected COVID-19 patients were admitted to the participating hospitals from 26 March 2021 to 30 July 2022. A total of (6875, 67%) PCR results were not reported and (1206, 12%) had negative PCR results. Only (2156, 21%) were confirmed to have SARS-CoV-2 infection by PCR, of whom (1387, 64%) had complete data and were included in the final analysis (figure 1).

Out of 1387 patients included in the analysis 48% (669/1387) were from MNH Dar es Salaam, 23% (313/1387), from KCMC in Moshi Kilimanjaro, 15% (209/1387) from MZRH in Mbeya, 8% (111/1387) from BMC in Mwanza region and 6% (85/1387) from BMH in Dodoma (figure 2).

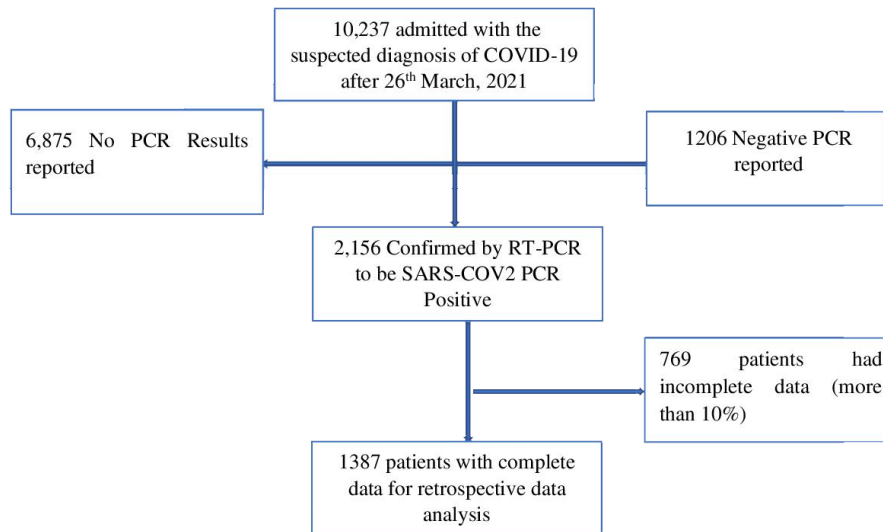
### Characteristics of the patients at admission to the hospital

#### Sociodemographic

The median age of the patients was 60 (19–102) years with (501, 36%) in the age group 60–74 years. More than half were males (722, 52%). Most of the patients had finished either primary (36, 26%) or secondary school (372, 27%). Nearly half (626, 45%) were covered by a health insurance (table 1). In-hospital mortality was (476, 34%) (table 1).

#### Comorbidities, symptoms, laboratory and radiologic findings at hospital admission

The most common comorbidities among the 1387 patients were hypertension (238, 40%) and DM (127, 40%). A total of 87 (6%) patients were HIV-infected. HIV VL was available for 19 patients only and was detectable in all of them (ie, >50 copies/mL) with the median VL,



**Figure 1** Patients screening and recruitment flow.

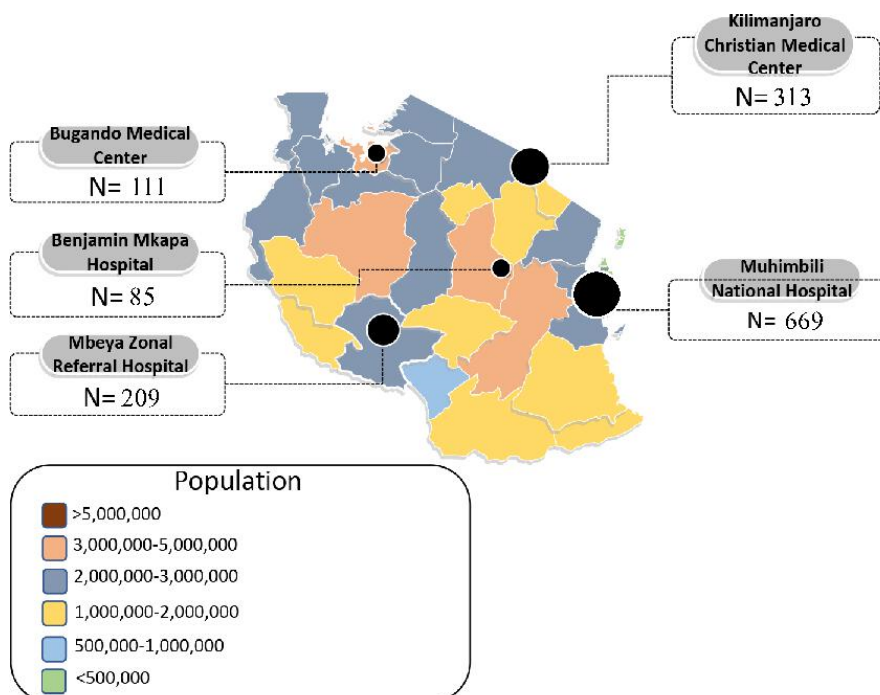
((IQR)=102 (20–226) copies/mL). CD4 count was available for 29 patients only and the median CD4 count, ((IQR)=136 (65–376) cells/mm<sup>3</sup>). The most common symptoms were dyspnoea (943, 68%), cough (889, 64%), fever (597, 43%), fatigue (570, 41%), chest pain (364, 26%) and headache (252, 18%). More than half of the patients had oxygen saturation (SpO<sub>2</sub>) of at least 95% (777, 56%). The number with tachypnoea was (138, 10%) and (683, 49%) had tachycardia. Almost half of the admitted patients (683, 49%) had lung infiltrates as reported in chest X-rays (online supplemental table 1).

**Hospital treatments received**

Although most of the patients had normal SpO<sub>2</sub> at admission (954, 69%) received supplemental oxygen during

their hospitalisation. Three-fourths received steroids (1038, 75%), (448, 32%) received ivermectin and (127, 9%) received remdesivir. Only (59, 4%) received invasive ventilation (online supplemental table 1).

There were many observations with missing data on the laboratory investigations as shown in table 2. However, patients who died compared with patients who survived had higher median values of CRP (median (IQR)=54.7 (14.8–124) mg/L, p=0.03); D-dimer (median (IQR)=4.4 (1.1–148.5) µ/mL, p=0.02); white cell count (WCC) (median (IQR)=9.6 (6.8–13.7) 10<sup>9</sup>/L, p<0.001); absolute neutrophil count (ANC) (median (IQR)=7.8 (4.9–11.2) 10<sup>9</sup>/L, p<0.001); fasting blood glucose (FBG) (median (IQR)=8.3 (6.2–13.9) mmol/L, p<0.001);



**Figure 2** Number of studied patients in each participating hospital and estimated population in the regions of domicile.



**Table 1** Sociodemographic characteristics at admission of patients hospitalised with COVID-19 at admission in Tanzania, 2021–2022, N=1387

Characteristic	Missing values	Died	Survived	Total	P value
		N=476 number (%)	N=911 number (%)	N=1387 Number (%)	
Age groups in years					
<45		90 (28)	236 (72)	326 (23)	<0.001
45–59		95 (27)	261 (73)	356 (26)	
60–74		182 (36)	319 (64)	501 (36)	
75–90		91 (51)	86 (49)	177 (13)	
>90	0	18 (67)	9 (33)	27 (2)	
Sex					
Male		261 (36)	461 (64)	722 (52)	0.14
Female	0	215 (32)	450 (68)	665 (48)	
Insurance					
Non-insured		287 (43)	385 (57)	672 (48)	
Insured	89	173 (28)	453 (72)	626 (45)	<0.001
Level of education					
No education		45 (53)	40 (47)	85 (6)	
Primary		115 (32)	254 (68)	360 (26)	<0.001
Secondary		141 (38)	231 (68)	372 (27)	
Postsecondary	209	85 (24)	276 (76)	361 (26)	
Occupation					
Unemployed		33 (40)	50 (60)	83 (6)	
Retired		64 (32)	134 (68)	198 (14)	
Employed	193	293 (32)	622 (68)	915 (66)	0.36
Marital status					
Living alone		97 (36)	174 (64)	271 (20)	0.23
Living with partner	89	282 (32)	612 (68)	894 (64)	

P values based on  $\chi^2$  test.

creatinine (median (IQR)=118 (87–177)  $\mu\text{mol/L}$ ,  $p<0.001$ ) and blood urea nitrogen (BUN) (median (IQR)=7.8 (5.6–12.2)  $\text{mmol/L}$ ,  $p<0.001$ ) (table 2).

### Results of multivariate models

In univariate analysis, mortality was associated with increasing age (with HRs increasing significantly with increasing age), lack of health insurance, HIV infection, chest pain, higher neutrophilia, no use of steroid and no use of ivermectin, all  $p$  values  $<0.05$  (online supplemental table 2). After controlling for other factors in multivariate analysis, compared with the age group of less than 45, the risk of dying was 1.64 times in age group 60–74 years, (aHR (95% CI)=1.64 (0.65 to 5.72),  $p=0.02$ ), almost three times in age group 75–90 years (aHR (95% CI)=2.7 (1.82 to 6.95),  $p=0.021$ ) and 4.4 times in elders above 90 years (aHR (95% CI)=4.4 (2.52 to 28.82),  $p=0.02$ ) (online supplemental table 2).

The risk of death was almost fourfold higher among uninsured patients compared with those with health insurance, (aHR (95% CI)=3.7 (1.09 to 14.25),  $p=0.04$ ).

The risk of death was twofold in patients with chest pain than patients without chest pain (aHR (95% CI)=2.27 (1.36 to 4.13),  $p=0.03$ ). The odds of death were over fourfold higher among patients with HIV coinfection compared with HIV negative (aHR (95% CI)=3.9 (1.46 to 8.15),  $p=0.03$ ). Higher level of neutrophils had a 12% increase risk of death compared with patients with low levels of neutrophils (aHR (95% CI)=1.12 (1.01 to 2.65),  $p=0.03$ ). No use of ivermectin had almost 80% chance of dying from COVID-19 (aHR (95% CI)=1.21 (1.04 to 1.57),  $p=0.04$ ). No use of steroid was associated with almost 60% mortality (aHR (95% CI)=1.36 (1.18 to 2.78),  $p=0.04$ ) (online supplemental table 2).

### DISCUSSION

We report on clinical manifestations and outcomes among 1387 patients admitted with confirmed COVID-19 to five hospitals in Tanzania.

One-third of COVID-19 patients died in the hospital. This is the same as the result of small single hospital study

**Table 2** Laboratory investigations of patients hospitalised with COVID-19 at admission, Tanzania, 2021–2022

Laboratory finding	Died Median (IQR)	Survived Median (IQR)	P value
CRP (mg/L), N=308	54.7 (14.8–124)	26.9 (9.8–94.7)	0.03
D-Dimer (µ/mL), N=373	4.4 (1.1–148.5)	3.3 (0.74–12.2)	0.02
Ferritin (ng/mL), N=390	745 (25.5–2000)	835.9 (317.5–1958.9)	0.8
ESR, N=129	68 (38–81)	45.5 (18.3–80.0)	0.6
WCC (×10 <sup>9</sup> /L), N=970	9.6 (6.8–13.7)	8.4 (5.8–11.4)	<0.001
ANC (×10 <sup>9</sup> /L), N=969	7.8 (4.9–11.2)	6.0 (4.1–8.4)	<0.001
ALC (×10 <sup>9</sup> /L), N=969	1.08 (0.6–1.9)	1.3 (0.8–2.25)	<0.001
Haemoglobin, (g/dL), N=971	12.2 (10.5–13.8)	12.6 (11.2–14)	0.005
Platelet (×10 <sup>9</sup> /L), N=961	239 (158–303)	249 (187–333.5)	<0.001
Fasting blood glucose (mmol/L), N=504	8.3 (6.2–13.9)	7.3 (5.8–10.0)	<0.001
LDH units/L, N=161	641 (298–1114)	787 (614–979)	0.3
Creatinine (µmol/L), N=353	118 (87–177.3)	91 (76–114.5)	<0.001
BUN (mmol/L), N=296	7.8 (5.6–12.2)	4.4 (3.4–7.0)	<0.001
AST units/L, N=192	52.5 (33.6–77.3)	43.1 (27 - 65)	0.4
ALT units/L, N=192	33.2 (20.2–47.9)	42.5 (25–71.1)	0.5
Cardiac troponin(pg/mL), N=94	0.6 (0.21–8.7)	0.36 (0.3–22)	0.3

P values based on  $\chi^2$  test.

ALC, absolute lymphocyte count; ALT, alanine aminotransferase; ANC, absolute neutrophil count; AST, aspartate aminotransferase; BUN, blood urea nitrogen; CRP, C reactive protein; D-Dimer, dimer that is a fibrin degradation product; ESR, erythrocyte sedimentation rate; LDH, lactate dehydrogenase enzyme; WCC, white cell count.

done in Dar es Salaam, Tanzania by Kassam *et al.*<sup>30</sup> and the one done in Kinshasha by Nlandu *et al.*<sup>29</sup> The HR of death increased significantly as patients age increased above 60 years. There were almost 1.6-fold increased risk of dying in the age group 60–74 years while the risk of dying was almost 4.4-fold in the age above 90 years. The relationship between age and COVID-19 deaths in this study reflects not only WHO data,<sup>1</sup> but also the findings of other studies of COVID-19 done elsewhere. For example, a study done in Sudan by Hasabo *et al.*<sup>5</sup> Lombardy Region, Italy by Cecconi *et al.*<sup>21</sup> and Grasselli *et al.*<sup>22</sup> indicated that majority of confirmed COVID-19 deaths were among patients aged above 60 years.

Similar to other studies,<sup>5 21 22</sup> the majority of patients in this study were male. Male sex has been found to be an independent factor associated with severe COVID-19 and mortality.<sup>14 15 41</sup> In our study, sex was not found to be an independent risk factor for death, though females had 43% lower chance of dying than male, but it was not statistically significant. This could be due to the fact that majority of study participants were older males and females with age above 60 years. This age group has more comorbidities which is a proxy to a severe COVID-19 and mortality for both males and females.

Patients who died were more likely to be unemployed, uninsured and with no formal education. The risk of death was almost fourfold in uninsured group compared with insured one. Being unemployed, no formal education and being uninsured are proxy indicators of poor

socioeconomic status which have been reported to be one of the risk factors for adverse outcomes and mortality from COVID-19.<sup>28 31</sup>

Obesity, diabetes and hypertension have been shown to increase the risk of developing more severe COVID-19 and mortality.<sup>42</sup> Data on obesity among COVID-19 patients were not recorded consistently in patients' file in our study. The leading comorbidities were hypertension followed by DM, though they were not found to be predictors of mortality in this study.

COVID-19 co-infected with HIV had almost fourfold of death compared with HIV negative. This finding seems to be higher than what was reported in a review published in *The Lancet* in May 2022 which showed 38% greater odds of in-hospital death for HIV-infected patients compared with HIV negative COVID-19 patients.<sup>43</sup> Again, the findings in t study have shown higher chance of death than the findings of a meta-analysis on the outcome of patients with COVID-19 and HIV coinfecting individuals which showed that individuals with HIV had increased chance of hospitalisation for COVID-19 with twofold increased risk of death regardless of CD4+ and HIV VL.<sup>44</sup> The higher HR of dying among COVID-19 coinfecting with HIV could be due to the fact that HIV regardless of CD4 count interferes body immunity.<sup>43 44</sup>

Almost two-thirds of admitted COVID-19 patients in this study presented with dyspnoea and cough which is similar to studies done elsewhere.<sup>18</sup> In contrast to the findings of our study which showed two-thirds of COVID-19

patients to have dyspnoea, other studies found only a quarter of the hospitalised patients had dyspnoea.<sup>14 15</sup> Perhaps because patients do not come to hospital till, they have severe symptoms. Other symptoms in order of importance were fever and fatigue which were present in almost half of patients, chest pain was present in a quarter of COVID-19 patients.

Fever was present in half of patients in our study, this was low compared with findings of studies done in Saudi Arabia, USA and China.<sup>11-13 45</sup> For example, a study of 370 000 confirmed COVID-19 patients in the USA, reported that fever was present in 70% of patients.<sup>45</sup>

Fatigue was found in almost half of our study patients, this is a bit higher compared with reports in other studies which showed fatigue to be in one-third of COVID-19 cases.<sup>14 15</sup> This could be due to the fact that patients came to the hospital late and in a severe form due to the denial of existence of COVID-19 by authorities in Tanzania during the second phase of the pandemic.

Fever, cough and arthritis appear to be protective factors in Cox regression. Fever, cough and arthritis are some of the early symptoms of SARS-CoV-2 infection and are, therefore, likely to be treated with over-the-counter medications early before patients succumb to severe disease.

Significantly, more deaths were observed in patients with chest pain. COVID-19 patients with chest pain were more than twice as likely to die compared with those without chest pain. Chest pain in COVID-19 has been strongly associated with worsening clinical outcomes in other previous studies.<sup>5 18</sup> Chest pain in COVID-19 patients occurs because of the virus-induced inflammatory responses leading to lung damage. The damage is evidenced by acute respiratory distress syndrome with diffuse alveolar damage, diffuse thrombotic alveolar microvascular occlusion and inflammatory mediator-associated airway inflammation.<sup>46 47</sup> The combination of these three pathogeneses impairs alveolar oxygenation, leads to hypoxaemia and respiratory acidosis and chest pain. If these hypoxic states are not treated may result in death from respiratory failure or sequelae of permanent lung damage.<sup>46-48</sup>

In this study, people who died had significantly higher median CRP, D-dimer, WCC, ANC, higher fasting blood glucose (FBG), serum creatinine, BUN compared with survivors.

Among the laboratory findings only ANC was found to be a predictor of mortality by at least 12%. This is in harmony with the findings of two studies from Wuhan China done by Yang *et al*<sup>1</sup> and Li *et al*<sup>41</sup> which reported that adverse outcome of COVID-19 was associated with neutrophilia.<sup>8</sup> Again higher absolute value of neutrophils could mean bacterial superinfection in COVID 19 patients, which perhaps increased the chance of mortality.

Half of COVID-19 patients in our study presented with lung infiltrates as reported by chest X-rays. Radiological documentation in this study did not take into account distribution of the opacities, however, more deaths were

observed among patients without opacification on chest X-rays without statistical significance. More than 50% of the patients' files in this study had no reported radiology findings.

Regarding treatment modalities that were given to admitted COVID-19 patients, three-quarters of patients received systemic steroids and supplemental oxygen. Ivermectin was used by 1/3rd of patients and only 1/10th used remdesivir.

The risks of death were found to be significantly lower in patients who used ivermectin. Patients who used ivermectin had a 21% chance of surviving compared with those who did not use it. Caly *et al* found that ivermectin can inhibit SARS-CoV-2 in vitro.<sup>38</sup> However, other studies and guidelines reported that there is no strong evidence to support use of ivermectin in COVID-19.<sup>49 50</sup>

In this study, we found that steroid use was protective against in-hospital mortality. The findings were the same as the results of review done by WHO Rapid Evidence Appraisal for COVID-19 Therapies Working Group.<sup>36</sup> Use of steroids is believed to reduce COVID-19-induced inflammatory response and hence halt the pathogenesis of the disease. This in turn reduces lung damage and improve clinical outcomes and prevent mortality.<sup>51</sup>

However, remdesivir use did not prevent mortality in our study in Tanzania. This could be due to low number (only 9%) of patients who used it in our patients.

Use of supplemental oxygen was associated with mortality in this study. The use of supplemental oxygen would mean more severe disease and it is well known that correcting hypoxaemia sometimes without hypoxia tends to have destructive effects and impairs lung healing.<sup>52 53</sup> Excessive and prolonged oxygen administration can lead to accumulation of reactive oxygen species which might lead to progressive destruction of alveolo-capillary membranes in the lungs and cause obstruction of lung capillaries which may form microthrombi, again due to damage of the alveoli air will lead to the surrounding tissues.<sup>53</sup> This lung damage by excessive oxygen in combination with COVID-19 can exacerbate cell apoptosis at the alveolar epithelium level resulting in more pulmonary injury and death may occur.<sup>52</sup>

The strength of this study is its multicentre across the country, thus having a national representation and a relatively larger sample size of COVID-19 than sample size in studies done in the same settings.<sup>29 30</sup>

The study has described clinical manifestations and outcomes of patients diagnosed with COVID-19 infection in Tanzania. However, the limitation of study was its retrospective nature which was based on documented patients' records, with a large number of patients left out of the analysis due to missed data, this might in a way affected some results of this study. Severity of COVID-19 might have been affected by variants of SARS-CoV-2 and COVID-19 vaccination which was not taken into account. However, COVID-19 vaccine was not available in Tanzania till September 2021. Most of COVID-19 admissions were in February–June, 2021. Therefore, COVID-19

vaccination might have not affected the results of this study.

## CONCLUSIONS

In this study, patients with COVID-19 presented more or less the same as patients elsewhere in the world, with dyspnoea, cough, fever, fatigue, chest pain and headache being the most presenting symptoms. Patients who died significantly had higher median value of CRP, D-dimer, WCC, ANC, higher FBG, serum creatinine and BUN. The independent predictors of mortality in this study were advanced age, HIV infection, no possession of a health insurance, chest pain, neutrophilia and no use of steroid or ivermectin. Clinicians should actively look for the predictors of mortality and take appropriate management to reduce mortality.

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