Comparative characterisation of COVID-19 patients with hypertension comorbidity in Malawi: a 1:2 matched retrospective case-control study

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ABSTRACT

Objective: The aim of this study was to characterize COVID-19 cases and explore the risk factors associated with mortality among hypertensive patients with COVID-19 across Malawi.

Methods: A retrospective case-control study design was used to provide a detailed account of cases and to explore the risk factors associated with mortality among hypertensive patients with COVID-19. In total, 441 patients were included in the study in a ratio of one case to two controls (1:2), matched by age.

Results: Deaths due to COVID-19 varied with hypertensive condition, with more deaths registered in hypertensive patients. Clinical signs and symptoms varied greatly between hypertensive and non-hypertensive COVID-19 patients, tending to be milder in the latter group. The risk of death due to COVID-19 among hypertensive patients increased with age, and was meaningfully associated with underlining comorbidities, such as HIV, TB, cardiovascular disease, and liver disease.

Conclusion: Our study revealed predictive factors for mortality in hypertensive COVID-19 patients, which can be used by policy makers and healthcare practitioners to identify those at a higher risk, and to determine the appropriate treatment approach to achieve the best possible clinical outcomes.

Introduction

In February 2020, the World Health Organization (WHO) designated the name coronavirus disease-2019 (COVID-19) to a clinical condition caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) (WHO, 2020). In the Malawian context, the first case was confirmed in Lilongwe on April 2, 2020, with more cases and deaths following over time (Chibwana et al., 2020; Chisale et al., 2021). According to a UNICEF situation report, as of January 13, 2021, Malawi had registered 9991 cases of COVID-19, including 275 deaths. Of these cases, 1844 were imported infections and 8147 were locally transmitted (UNICEF Malawi, 2021).

Covid-19 in Wuhan, China, old age, chronic major comorbidities, and male sex have consistently been associated with increased mortality (Chen et al., 2020). Hypertension has been reported as the most common comorbidity for patients with COVID-19, resulting in cases with more severe symptoms and higher mortality (Wang et al., 2021).

In a study conducted in China, out of 20 982 patients with COVID-19, 12.6% suffered from hypertension, which was the most frequent coexisting condition (Zhou et al., 2020). In the same study, it was reported that among those patients who died of COVID-19, the proportion of those with hypertension ranged from 6.0% to 36% (Zhou et al., 2020). Aside from old age, male gender, respiratory diseases, diabetes, and cardiovascular diseases such as hypertension were reported to be strong predictors of worse clinical outcomes in COVID-19 patients (Zhou et al., 2020).

As of January 31, 2021, 23 963 people had been infected with COVID-19 across Malawi (Ministry of Health Malawi, 2021; Worldometer, 2021), with 1017 hospital admissions and 345 deaths. However, there is paucity of data on outcomes for hypertensive hospitalized COVID-19 patients in Malawi. Furthermore, predictors of mortality among hypertensive patients with COVID-19 are unknown. The aim of this study was to characterize COVID-19 cases and to explore the risk factors associated with mortality among hypertensive COVID-19 patients across Malawi.
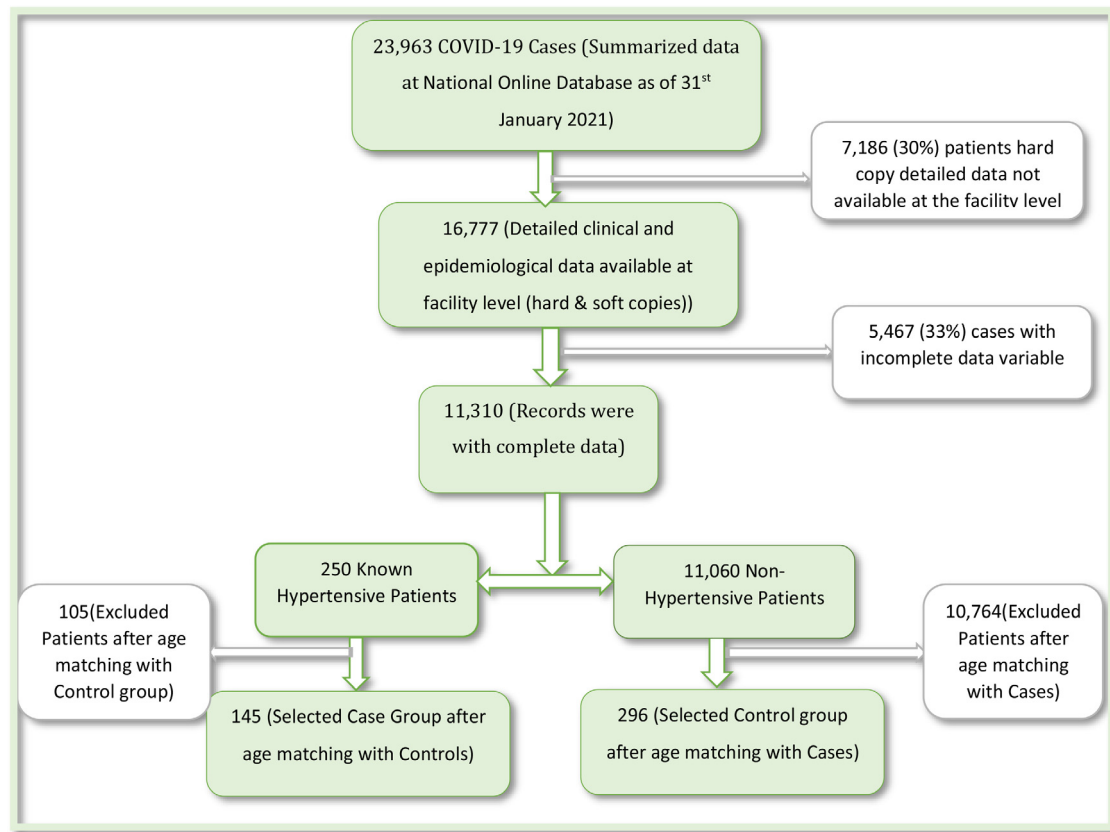
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Figure 1. Profile of hypertensive and non-hypertensive COVID-19 patients.

Methods

Study design and settings

This study used a retrospective case-control study design. The focus was on all complete records of Covid-19 patients with hypertension and their controls in the ratio of 1:2 and matched by age, obtained from hospitals under ministry of health. Increasing the ratio to one case to two controls helped to increase the power of the study (Stürmer, 2001). Moreover, matching the cases to controls by age helped to reduce the confounder effect, because hypertension is directly correlated with increasing age (Lenfant, 1990).

Population, sample size, and data collection

The cases for our study were based on the records of all patients who had COVID-19 and hypertension in Malawi between April 6, 2020 and January 31, 2021. The controls comprised COVID-19 patients without hypertension within the same specified time period as the cases. Epidemiological and clinical data, including those on chronic illnesses, were extracted from the medical registry/case file and nationally designed line listing (See supplementary documents). A census approach was used to identify all hypertensive COVID-19 patients cases for inclusion. A systematic random sampling technique was used to select the controls (COVID-19 patients without hypertension).

In total, 441 patients were included in the study, comprising 145 cases and 296 controls matched by age in a ratio of 1:2 (Figure 1).

The inclusion criteria were as follows: cases — COVID-19 patients with a known and confirmed hypertensive condition; controls — any COVID-19 patients without hypertension. Those with incomplete records were excluded.

A diagnosis of hypertension was confirmed by a qualified clinician and documented in the patient's file and health passport. For both cases and controls, SARS-CoV-2 infection was confirmed by RT-PCR, using swab samples from the upper respiratory tract (nasopharyngeal/oropharyngeal) or from the lower respiratory tract (sputum/endotracheal aspirate). Tests were carried out using the Abbott m2000 SARS-CoV-2 Real Time PCR Detection Kit.

Ethical approval to conduct this study was obtained from the National Health Science Research Committee (NHSRC) (protocol # NHSRC20/11/2630). Clearance was obtained from the Ministry of Health. No name or any other identifiable information for the patients was indicated on the data collection form, which the authors adapted from one produced by the Ministry of Health. Data were extracted from the medical files/forms by research assistants, who were trained for 3 days prior to data collection.

Data analysis

Data were analyzed using Statistical Product and Service Solutions (SPSS) version 25.0 (SPSS Inc., Chicago, IL, USA). Quantitative variables were expressed as means ± standard deviations, while qualitative variables were expressed as frequencies and percentages. A non-parametric Mann–Whitney U-test was used to compare quantitative variables between hypertensive and non-hypertensive groups. The chi-square test was used to evaluate categorical data. A post-hoc test employing a Bonferroni method was applied to the p-values obtained from the chi-square tests performed on the different categorical variables. Multivariable Cox regression analyses were used to investigate the risk factors associated with COVID-19 deaths. P-values < 0.05 were considered significant.

Results

The mean age of all COVID-19 patients was 52.3 (± 15.6) years, and did not vary significantly between the hypertensive and non-hypertensive groups (Table 1). The majority of COVID-19 patients were

Table 1
Demographic and epidemiological characteristics of hypertensive patients with COVID-19

Variables	All patients (441)	Hypertension group (145)	Non hypertension group (296)	*p*-value
Age	52.3 ± 15.6	52.2 ± 14.9	52.4 ± 16.0	0.69
Gender				
Male	289 (65.5)	89 (61.4)	200 (67.6)	0.19
Female	152 (34.5)	56 (38.6)	96 (32.4)	
Transmission				
Local	425 (96.4)	141 (97.2)	284 (95.9)	0.49
Imported	16 (3.6)	4 (2.8)	12 (4.1)	
Hospitalized	34 (7.7)	25 (17.2)	9 (3.0)	< 0.001
Mechanical ventilation	15 (3.4)	11 (7.6)	4 (1.4)	< 0.001
Health outcome				
Death	21 (4.8)	14 (9.7)	7 (2.4)	<
Recovered	420 (95.2)	131 (90.3)	289 (97.6)	0.001

Table 2
Clinical characteristics of hypertensive patients with COVID-19

Variables	All patients (*N* = 441)	Hypertension group (*n* = 145)	Non hypertension group (*n* = 296)	*p*-value
Signs and symptoms				
Fever	236 (53.5)	77 (53.1)	159 (53.7)	0.9
Loss of smell/taste	122 (27.7)	12 (8.3)	110 (37.2)	< 0.001
Cough	277 (62.8)	97 (66.9)	180 (60.8)	0.21
Shortness of breath	128 (29.0)	50 (34.5)	78 (26.4)	0.08
Breathing difficulty	59 (13.4)	12 (8.3)	47 (15.9)	0.03
Stiff nose	21 (4.8)	1 (0.7)	20 (6.8)	0.005
Sore throat	47 (10.7)	9 (6.2)	38 (12.8)	0.03
Runny nose	38 (8.6)	4 (2.8)	34 (11.5)	0.002
Chest pain	118 (26.8)	28 (19.3)	90 (30.4)	0.01
Nausea	39 (8.8)	4 (2.8)	35 (11.8)	0.002
GBW	106 (24.0)	15 (10.3)	91 (30.7)	< 0.001
Headache	165 (37.4)	44 (30.3)	121 (40.9)	0.03
Abdominal pain	23 (5.2)	12 (8.3)	11 (3.7)	0.04
Vomiting	16 (3.6)	5 (3.4)	11 (3.7)	0.89
Comorbidities				
Diabetes	48 (10.9)	38 (26.2)	10 (3.4)	< 0.001
HIV	19 (4.3)	14 (9.7)	5 (1.7)	< 0.001
Asthma	12 (2.7)	8 (5.5)	4 (1.4)	0.01
COPD	3 (0.7)	2 (1.4)	1 (0.3)	0.21
TB	2 (0.5)	2 (1.4)	0	0.04
Stroke	1 (0.2)	1 (0.7)	0	0.15
Cardiovascular disease	2 (0.5)	1 (0.7)	1 (0.3)	0.61
Liver disease	2 (0.5)	1 (0.7)	1 (0.3)	0.61
Kidney disease	1 (0.2)	1 (0.7)	0	0.15

males (65.5%) (Table 1). Hospitalization and mechanical ventilation requirements for COVID-19 cases were significantly higher among those with hypertension. More deaths were reported among COVID-19 cases with hypertension (17; *n* = 21; *p* < 0.001) (Table 1).

In this study, the reported signs and symptoms due to SARS-CoV-2 infection were loss of smell or taste, difficulty in breathing, stiff nose, sore throat, runny nose, chest pain, nausea, general body weakness, headache, and abdominal pain. These clinical signs and symptoms of COVID-19 varied greatly across both hypertensive and non-hypertensive patient groups, although they tended to be milder in the non-hypertensive patients. However, the prevalence of abdominal pain was significantly higher among COVID-19 patients with hypertension (Table 2). Furthermore, diabetes, HIV, asthma, and tuberculosis were more prevalent among hypertensive COVID-19 patients (Table 2). The Cox proportional hazard regression model results revealed that the risk of COVID-19 deaths among hypertensive patients increased with age, and was meaningfully amplified by underlining comorbidities such as HIV, TB, cardiovascular disease, and liver disease (Table 3).

Discussion

Despite several reports indicating the need for characterization of COVID-19 cases in particular settings (Chisale et al., 2020, 2021; Salyer et al., 2020; Vallverdu et al., 2021), to date there has been

Table 3
Multivariate Cox regression analysis of clinical characteristics of hypertensive and non-hypertensive patients with COVID-19

Variable	Multivariable OR (95% CI)	*p*-value
Age	1.06 (1.03–1.09)	< 0.001
Gender	1.55 (0.62–3.86)	0.35
Diabetes	1.02 (0.31–3.39)	0.97
HIV	0.24 (0.07–0.86)	0.03
TB	0.03 (0.00–0.25)	< 0.001
Cardiovascular disease	0.11 (0.01–0.83)	0.03
Liver disease	0.04 (0.01–0.35)	0.00

no comprehensive, nationwide Malawian study on the risk factors for COVID-19 patients with hypertension. Furthermore, most of the published data are from Europe, Asia, America, and other non-African settings (Clark et al., 2021; Hosseinzadeh et al., 2021; Lavery et al., 2021; Shibata et al., 2020; Tadic et al., 2021; Wang et al., 2021), making it unfeasible for African countries to formulate policies and strategies for fighting the COVID-19 pandemic based local studies.

Our 1:2 case-control study, matched by age, comprised 441 confirmed COVID-19 patients, with 145 (32.9%) known to be hypertensive. Using nationwide data, the clinical and epidemiological characteristics of confirmed hypertensive COVID-19 patients were compared with those

of non-hypertensive patients, thus establishing some important risk factors predictive for mortality among hypertensive COVID-19 patients.

The mean age of all COVID-19 patients included in this study was 52.3 ($\pm$ 15.6) years; as expected, the mean age did not vary. This is not surprising, as most developing countries have a youthful population. The hypertensive condition varied significantly among those hospitalized and under mechanical ventilation. The hypertensive condition was significantly linked with death among COVID-19 cases.

Studies from different settings have shown certain clinical parameters to be predictors of worse clinical outcomes in COVID-19 patients (Salyer et al., 2020; Vallverdu et al., 2021; Yin et al., 2021; Zhou et al., 2020). Notable factors that appear to be related with severe COVID-19 include, old age, male gender, cardiovascular diseases, respiratory diseases, and diabetes (Zhou et al., 2020). Earlier studies focused mostly on descriptions of different comorbidities, including the influence of these various risk factors on susceptibility, severity, and mortality among COVID-19 patients. More recently, however, some studies have focused on a particular risk factor, with hypertension being one of the most reported (Clark et al., 2021; Hosseinzadeh et al., 2021; Shibata et al., 2020; Tadic et al., 2021; Wang et al., 2021). Unfortunately, none of these studies was based in the African region.

The findings from our study showed that loss of smell or taste, difficulty in breathing, stiff nose, sore throat, runny nose, chest pains, nausea, general body weakness, headache, and abdominal pain were clinical signs and symptoms of COVID-19 that varied significantly, regardless of the hypertensive or non-hypertensive condition among patients, with the exception of abdominal pain, which was highly prevalent among COVID-19 patients with hypertension. However, in contrast to our findings, a study from Iran by Ramin et al. (2021) found that fever and shortness of breath were more prevalent among COVID-19 patients with hypertension (Hosseinzadeh et al., 2021). This disparity could be due to differences in SARS-CoV-2 variants circulating in different regions of the world, or may be due to the varying characteristics of the populations involved somehow affecting the manifestation of disease. Therefore, there is a need to focus studies on particular populations in order to identify the characteristics of their cases, and allow appropriate policy formulation (Chisale et al., 2021; Salyer et al., 2020).

In line with other studies, the COVID-19 cases among the hypertensive patients were significantly associated with diabetic condition. This could be because diabetes and hypertension are commonly related in terms of their pathophysiology (Gesesew et al., 2021). However, unlike most of the findings from other studies (Clark et al., 2021; Hosseinzadeh et al., 2021; Shibata et al., 2020; Tadic et al., 2021; Wang et al., 2021), our study showed that most patients with hypertension had HIV, asthma, and tuberculosis. Although this may need further investigation and confirmation, as well as more understanding of the pathophysiological relationship, it is known fact that HIV/AIDS and TB are very common in developing countries, and hence more likely to be prevalent (Chisale et al., 2021). Furthermore, HIV/AIDS is known to have an influence on the whole immune system, as well as multiple systems of the body.

Our study revealed that the risk of COVID-19 deaths among hypertensive patients increased with age, and was meaningfully amplified by HIV, TB, cardiovascular disease, and liver disease. Some studies have equally shown that cardiovascular diseases pose a higher risk for death among hypertensive COVID-19 patients (Hosseinzadeh et al., 2021; Wang et al., 2021). However, so far, no study has indicated HIV and TB as risk factors for increased mortality among hypertensive patients infected with COVID-19. It is concerning to learn that local programmes responsible for HIV and TB are being critically affected by COVID-19, thus posing additional challenges for those with these comorbidities (Thekkur et al., 2021). Therefore, the Malawian authorities may need to consider these risk factors when handling COVID-19 cases with hypertension.

Study strengths and limitations

By applying a case-control ratio of 1:2, matched by age, our study avoided imbalances and potential confounding issues caused by other known risk factors, including age. The consequent reduction in variability thus increasing efficiency. However, our results must be interpreted with caution because the study employed a retrospective design in which some factors were out of the researchers' control. This important issue meant that some variables could not be included for analysis. Furthermore, the retrospective case-control design did not allow direct analysis of incidence or temporal relationships, and was subject to selection bias with regard to controls. Thus, although the case-control analysis was matched by age, the authors did not match by time. This may have introduced bias because COVID-19 care might have improved over time. However, as a nationwide COVID-19 data study, it may still reflect and confirm the outcomes of COVID-19 infection in patients with hypertension in Malawi.

Conclusion

This study revealed that the risk of COVID-19 deaths among hypertensive patients increased with age, and was meaningfully amplified by HIV, TB, cardiovascular disease, and liver disease. The consequent characterization of Malawian COVID-19 patients with hypertension will be able to guide our local policies and efforts. Furthermore, our study revealed predictive factors for mortality in COVID-19 that can be used by healthcare practitioners to identify high-risk hypertensive COVID-19 cases, and to determine appropriate treatment approaches in order to achieve the best possible clinical outcomes.

Data availability

The data for the study are available from the corresponding author on reasonable request.

Ethical approval

Ethical approval to conduct the study was obtained from the National Health Science Research Committee (NHSRC), protocol # NHSRC20/11/2630.

Consent

Written or oral informed consent was waived by the NHSRC.

Conflicts of interest

The authors declare no conflicts of interest.

Funding

Authors' contributions

Study conception: MROC, BWN, CM, PK, and BCM. Study design: MROC, BWN, CM, PK, and BCM. Data collection: MROC, BWN, CM, PK, and BCM. Data analysis: MROC, BWN, CM, PK, SEM, and BCM. Manuscript preparation: MROC, BWN, CM, PK, SEM, and BCM. All the authors contributed towards the completion of this study, and read and approved the manuscript.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijregi.2021.11.005.

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