Received: 28 October 2021 | Revised: 4 December 2021 | Accepted: 10 December 2021

DOI: 10.1111/jch.14417

ORIGINAL ARTICLE

WILEY

Mortality associated with COVID-19 and hypertension in sub-Saharan Africa. A systematic review and meta-analysis

Ben Bepouka MD, MSc[1] | Hippolyte Situakibanza MD, PhD[1] | Modibo Sangare MD, PhD[2] | Madone Mandina MD, PhD[1] | Nadine Mayasi MD, MPH[1] | Murielle Longokolo MD[1] | Ossam Odio MD[1] | Donatien Mangala MD[1] | Fiston Isekusu MD[1] | Jean Marie Kayembe MD, PhD[3] | Jean Nachega MD, PhD[4] | Marcel Mbula MD[1]

[1] Infectious Diseases Unit, Kinshasa University Hospital, Faculty of Medicine, University of Kinshasa, Democratic Republic of Congo, Kinshasa, USA

[2] Faculty of Medicine and Odontostomatology (FMOS), University of Sciences, Techniques & Technologies of Bamako (USTTB), Bamako, Mali

[3] Pneumology Unit, Kinshasa University Hospital, Faculty of Medicine, University of Kinshasa, DRC, Kinshasa, USA

[4] Department of Medicine, Centre for Infectious Diseases, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa; and Department of Epidemiology, Infectious Diseases and Microbiology, University of Pittsburgh, Pittsburgh, Pennsylvania, USA

Correspondence
Ben Bepouka MD, Infectious Diseases Unit, Kinshasa University Hospital, Faculty of Medicine, University of Kinshasa, Democratic Republic of Congo.
Email: benbepouka@gmail.com

Abstract

Hypertension is a common comorbidity in COVID-19 patients. However, little data is available on mortality in COVID-19 patients with hypertension in sub-Saharan Africa (SSA). Herein, the authors conducted a systematic review of research articles published from January 1, 2020 to July 1, 2021. Our aim was to evaluate the magnitude of COVID-19 mortality in patients with hypertension in SSA. Following the PRISMA guidelines, two independent investigators conducted the literature review to collect relevant data. The authors used a random effect model to estimate the odds ratio, or hazard ratio, with a 95% confidence interval (CI). Furthermore, the authors used Egger's tests to check for publication bias. For mortality analysis, the authors included data on 29 945 COVID-19 patients from seven publications. The authors assessed the heterogeneity across studies with the I^2 test. Finally, the pooled analysis revealed that hypertension was associated with an increased odds of mortality among COVID-19 inpatients (OR 1.32; 95% CI, 1.13–1.50). Our analysis revealed neither substantial heterogeneity across studies nor a publication bias. Therefore, our prespecified results provided new evidence that hypertension could increase the risk of mortality from COVID-19 in SSA.

KEYWORDS
Africa, COVID-19, hypertension, mortality

1 | INTRODUCTION

Coronavirus disease 2019 (COVID-19), a new emerging acute respiratory disease, is transmitted mainly through respiratory droplets and results in the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). As of July 22, 2021, COVID-19 has affected 42 385 317 people worldwide, with 650 684 deaths. In Africa, COVID-19 accounted for 4 634 617 infections with 109 711 deaths, a case fatality rate of 0.23%.[1] In symptomatic patients with COVID-19, the clinical presentation is mild in 80%, moderate to severe in 15%, and critical in 5%.

Severe cases are at risk of developing acute respiratory distress syndrome (ARDS), shock, thromboembolic events, multi-visceral failure, and death.[2]

Hypertension affects more than 1 billion people worldwide, which makes it one of the most important public health problems globally.[3] However, our knowledge of the impact of hypertension on SARS-CoV-2 infection is limited, especially in sub-Saharan Africa. Several clinical studies have shown that hypertension is one of the most common comorbidities in patients with SARS-CoV-2.[4–6] A cohort study on 1099 ambulatory and hospitalized patients with COVID-19 found a history of hypertension in 15% of the patients.[7]

Few meta-analyses have established the association between hypertension and mortality in patients with COVID-19 across the world.[8–13] However, Africa has often been omitted in these meta-analyses. As of July 22, 2021, we did not find a single meta-analysis from Africa on the association between hypertension and mortality in patients with COVID-19. In sub-Saharan Africa (SSA), several observational studies were conducted on the predictors of mortality in patients with COVID-19 to determine the contribution of hypertension as a comorbidity to COVID-19 mortality. The results were discordant. Some African studies have found hypertension to be a predictor of mortality,[14–16] while others have not.[17–21] These studies had different study designs and study populations and have therefore produced different estimates and effect sizes. Consequently, a comprehensive and systematic analysis was needed to minimize such variability. In this review paper, we conducted a systematic review and meta-analysis, the first in SSA to our best knowledge, to investigate the association between hypertension and mortality in patients with COVID-19 in SSA. We hypothesized that hypertension would be significantly associated with mortality in COVID-19 patients in Africa.

2 | METHODS

2.1 | Data sources

We followed Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and conducted a systematic review using PubMed, Google Scholar, and Web of Science between January 1, 2020, and July 1, 2021.

We conducted our literature search on Pubmed as follows. We first searched for our key words individually (COVID-19, hypertension, mortality, Sub-Saharan Africa*). For each key word, we used synonyms : COVID-19 OR SARS-CoV-2; hypertension OR high blood pressure; mortality OR lethality OR fatal outcome; Sub-Saharan Africa* OR "Africa South of the Sahara"* OR Central Africa* OR Western Africa* OR Eastern Africa* OR Southern Africa* OR Benin* OR*Tanzania* OR Togo* OR Uganda* OR Zimbabwe* OR Cameroon* OR Cape Verde* OR Congo * OR Democratic republic of the Congo* OR Cote d'Ivoire* OR Ghana* OR Lesotho* OR Mauritania* OR Nigeria* OR Atlantic Islands* OR Senegal* OR Sudan* OR South Sudan* OR Swaziland* OR Zambia* OR Angola* OR Botswana* OR Gabon* OR Mauritius* OR Namibia* OR Seychelles* OR South Africa* OR Equatorial Guinea*OR Benin* OR Burkina Faso* OR Burundi* OR Central African Republic* OR Chad* OR Comoros* OR "Democratic Republic of the Congo"* OR Eritrea* OR Ethiopia* OR Gambia* OR Guinea* OR Guinea-Bissau* OR Kenya* OR Liberia* OR Madagascar* OR Malawi* OR Mali* OR Mozambique* OR Niger* OR Rwanda* OR Sierra Leone* OR Somalia*. Then, we used the advanced search to combine all four key words with AND between two key words and OR between synonyms. Two independent investigators reviewed selected review papers for relevance to the abstract. We evaluated the full text based on the inclusion and non-inclusion criteria.

2.2 | Study selection

Two independent investigators selected potentially eligible studies based on the appropriateness of the title and abstract. They then reviewed the full texts according to the eligibility criteria. Reviews, editorials, case reports, and family studies were not included for the analysis. Clinical studies that did not clearly indicate death as an outcome were also not included. In cases where the same author had more than one study on the same patient (duplicate publications), we included only the paper with the highest quality (Figure 1).

2.3 | Data extraction

Two investigators independently used our data extraction form, which included information on authors, year of publication, country, study design, study location (number of study sites), sample size, age, sex, outcome, mortality rate, history of hypertension, diabetics, cardiovascular disease, and chronic lung disease. This information was obtained independently by two investigators. A third investigator double checked the filled data extraction forms for completion, and compared the data per review paper to remove duplicates and resolve any discrepancies.

2.4 | Quality assessment

Two independent reviewers used the methodological items for non-randomized studies (MINORS) list (Table 1) to assess the methodological quality of individual studies. Each of the 12 MINORS items was scored with 0 points if not reported, 1 point if inadequately reported, and 2 points if adequately reported, which made a total of 24 points maximum. A study was labeled either "high quality" if the total score was ≥ 17 or "low quality" if the total score was < 17.[22–23]

2.5 | Data analysis

We did statistical analysis using STATA software version 14 and used the odds ratio (OR) or hazards ratio (HR) with a 95% confidence interval (CI) to estimate the correlation between hypertension and mortality in patients with COVID-19. We assessed heterogeneity across studies using the I^2 statistic and the X^2 test. For the X^2 test,

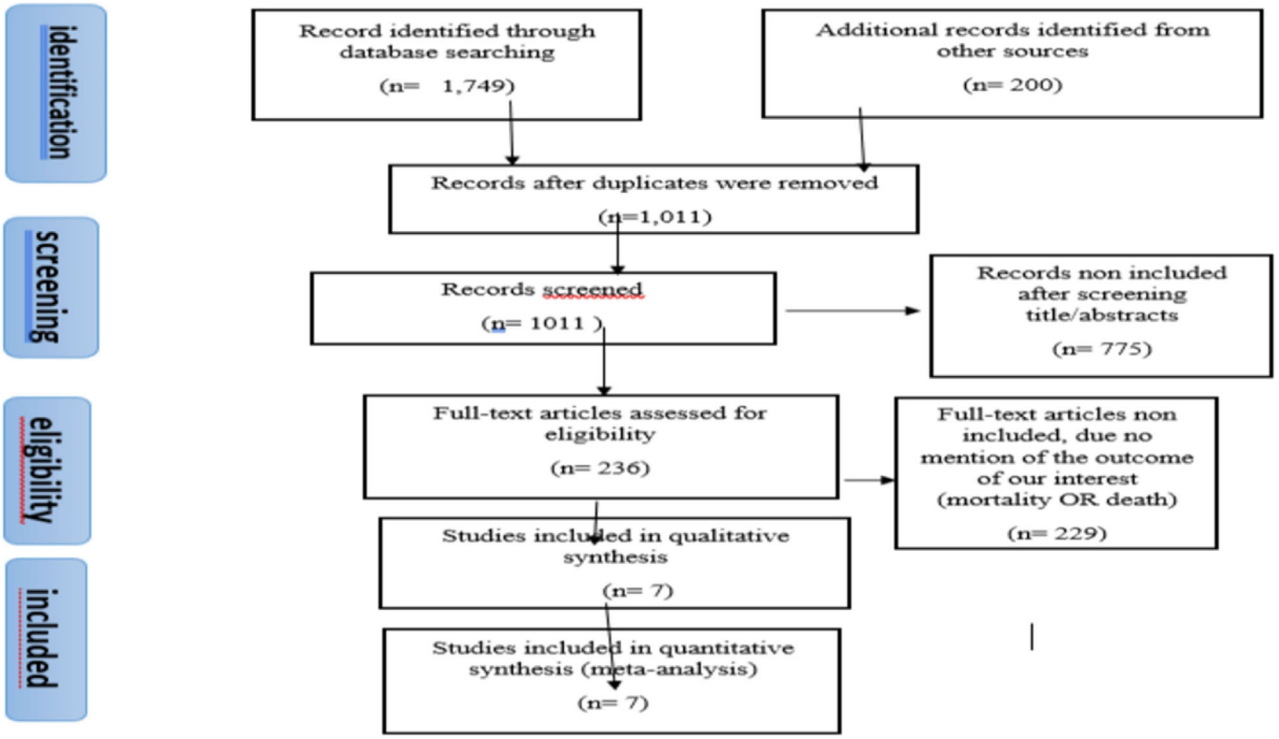

FIGURE 1 Flowchart showing the selection of studies for the meta-analysis of the association of hypertension with COVID-19 mortality in sub-Saharan Africa

TABLE 1 Methodological items for nonrandomized studies (MINORS)

Item number	Item description	Item number	Item description
1	A clearly stated aim	9	An adequate control groups
2	Inclusion of consecutive patients	10	Contemporary groups
3	Prospective collection of data	11	Baseline equivalence of groups
4	Endpoints appropriate to the aim of the study	12	Adequate statistical analysis
5	Unbiased assessment of the study endpoint		
6	Follow-up period appropriate to the aim of the study		
7	Loss to follow-up less than 5%		
8	Prospective calculation of the study size		

significant heterogeneity between studies was indicated by a Cochran's Q p value < .10. Heterogeneity was considered low if the I^2 value was less than 25%, moderate if the I^2 value was from 25% to 50%, or high if the I^2 value was greater > 50% .[24] In the case of high heterogeneity, we did a sensitivity analysis and had to remove a study from the meta-analysis.[25] We used forest plots to show visually the effect estimates of the included studies. We used Egger's test to assess a potential publication bias. A $p < .05$ at both ends was considered statistically significant.

3 | RESULTS

3.1 | Study selection and characteristics

The flow chart shows the studies in our meta-analysis (Figure 1). A total of seven studies (all retrospective except one and all of high quality) involving 29 945 patients from eight Sub-Saharan African countries were finally included in our study. Based on the criteria described previously (Table 1). The studies were published from January 2020 to July 2021. The number of confirmed COVID-19 cases in each study ranged from 105 to 22 308. All the included studies in the meta-analysis were retrospective (Table 2). The proportion of patients with hypertension ranged from 1.18% to 34%.

3.2 | Mortality analysis

Patients with COVID-19 and hypertension had an increased probability of death as compared to those without hypertension. OR = 1.32; $_{95\%}$ CI [1.13–1.50] (Figure 2).

TABLE 2 Characteristics of the included study

First author and year of publication	Country	Study site	Sex ratio	Age [median, interquartile range]	Sample size	Mortality rate* (%)	Diabetes n (%)	Hyper-tension n (%)	Cardiovascular diseases n (%)	Chronic pulmonary diseases n (%)
Matangila et al., 2020	DRC	One hospital in Kinshasa	1.04	54 years old [38-64]	160	20	31 (19)	55 (34)	11 (7)	5 (3)
Nachega et al., 2020	DRC	Seven largest health facilities in Kinshasa	1.90	46 years old [34-58]	766	13.2	107 (14)	194 (25.4)	30 (3.9)	26 (3.4)
Abraha et al., 2021	Ethiopia	One district health center in Mekelle city	1.72	29 years old [24-38]	2617	0.8	82 (3.1)	82 (3.1)	–	73 (2.8)
Jaspard et al., 2021	Guinea and Burkina	Three hospitals in Burkina and Guinea	1.77	41 years old [30-57]	1805	29	219 (12)	386 (21)	–	–
Osibogun et al., 2021	Nigeria	10 health centers in Lagos	1.92	43 years old [35-55]	2184	3.3	149 (6.8)	365 (16.7)	2 (2.22)	–
Ghada	Sudan	One health center	1.69	–	105	29	53 (49)	53 (49)	–	–
Boule et al., 2020	South Africa	western Cape Provincial Health Centers of Public sector health	0.85	–	22308	2.8	3123 (14)	5131 (23)	–	1562 (7)

*The only outcome was mortality in all seven selected studies that were all retrospective except one.

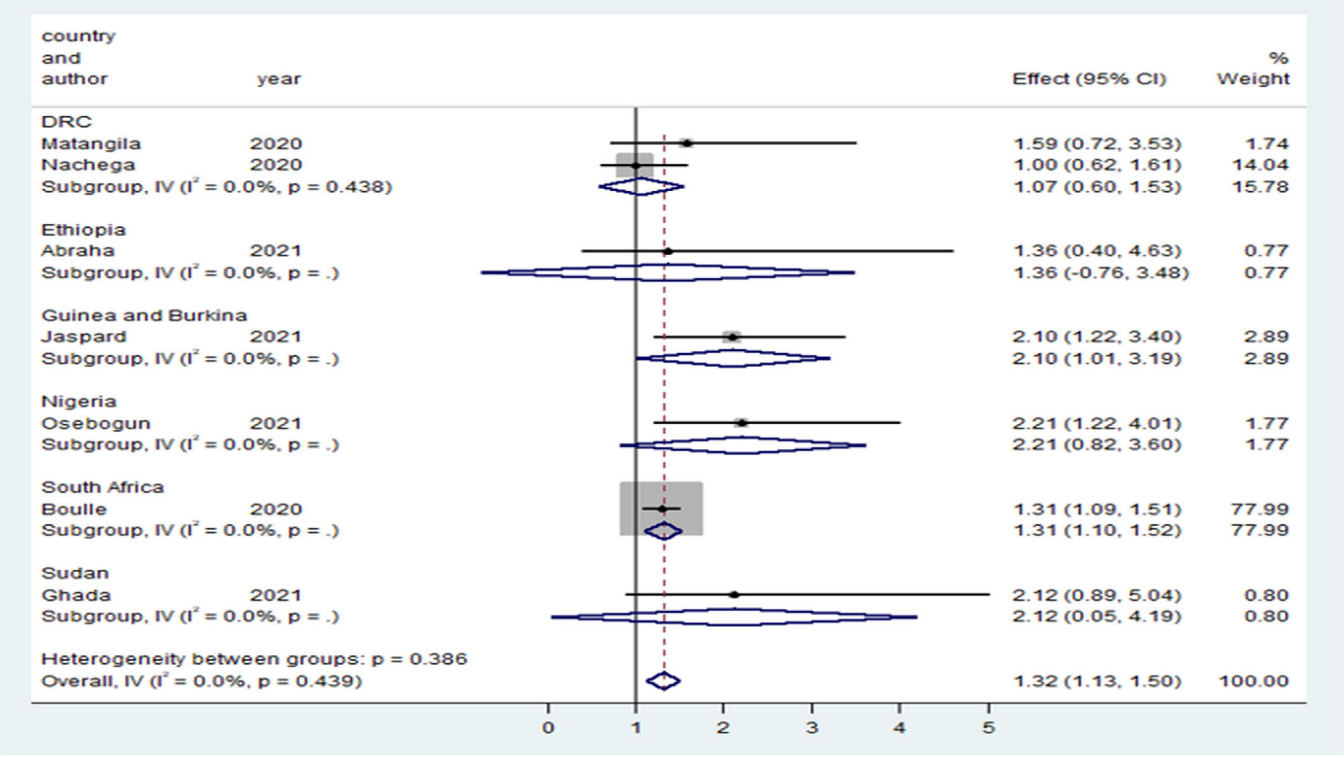

FIGURE 2 Forest plot for the association between hypertension and mortality in patients with COVID-19

TABLE 3 Egger's test to analyze selected review papers for publication bias

Standard effect	Slope	Bias
Coefficient	0.19	0.87
Standard error	0.12	0.67
T	1.57	1.29
p value	0.177	0.254
95% IC Confidence interval	−0.13 – 0.52	−0,87 – 2.61

3.3 | Heterogeneity across studies

No heterogeneity was evident between studies ($I^2 = 0.0\%$, Cochran Q test 5.82 $p = 0.439$) (Figure 2).

3.4 | Publication bias

Egger's test found no publication bias ($p = .254$) (Table 3).

4 | DISCUSSION

In our meta-analysis, we found that the risk of death was higher in hypertensive patients with COVID-19 as compared to non-hypertensive ones. It has been shown that

Hypertensive patients tend to be severely affected and are more likely to die from COVID_19. Among possible mechanistic explanations for such an association, angiotensin converting enzyme (ACE2) could most likely be involved. Indeed, ACE2 is a type 1 integral membrane glycoprotein in the epithelial cells of multiple organs (heart, kidney, lung, and stomach). There are several situations that can promote overexpression of ACE2. Firstly, arterial hypertension itself leads to an increased activation of the renin-angiotensin system (RAS). Secondly, regular use of antihypertensive drugs such as angiotensin II receptor blockers (ARB) and ACE inhibitors increases the expression of ACE2. These two mechanisms may synergistically interact in a hypertensive patient taking such antihypertensive medication. The overexpression of ACE2 facilitates the entry of SARS-CoV-2 into pneumocytes.[26] Such enhanced viral uptake favors respiratory infection, which significantly increases the severity and mortality rate of COVID-19 in hypertensive patients taking ARBs and/or ACEIs.[27] After viral uptake, ACE2 overexpression, which is thought to provide lung protection, is downregulated as the enzyme is decreased, resulting in reduced angiotensin II degradation, increased aldosterone secretion, and loss of potassium from the urine and subsequent hypokalemia.[28]

The association between hypertension and mortality was stronger in studies with a high proportion of male patients with COVID-19. Almost all the studies in the meta-analysis had a male predominance. It is known that males are more exposed to severe COVID-19. A greater expression and activation of angiotensin II type I receptor (AT1R) has been observed in hypertensive male patients, most likely due to vasoconstriction, a proinflammatory response, with increased oxidative stress, leading to acute respiratory distress syndrome (ARDS).[29] This condition helps explain the higher incidence of severe COVID-19 in males as compared to females. Estrogen has been thought to predispose females to a "good" renin-angiotensin-aldosterone system (RAS).[30]

Most of our studies had patients with a median age greater than 40 years old. It is known in the literature that older individuals with hypertension have lower ACE2 levels and higher RAS signaling, leading to increased hypertension. A higher RAS signaling that evolves to extremely low ACE2 levels and markedly elevated RAS signaling after COVID-19 infection results in a more severe disease. In contrast, younger individuals without hypertension have higher ACE2 and lower RAS signaling, which progresses to slightly lower ACE2 levels and slightly increased RAS signaling after COVID-19 infection, resulting in a potentially higher disease incidence but less severe disease.[31]

Diabetes mellitus, cardiovascular disease, and chronic lung disease were the main co-morbidities in patients with COVID-19. A recent study found that hypertension alone was not an independent predictor of disease outcome, but only in association with diabetes mellitus or another risk factor .[32] Importantly, some studies have found that hypertension and diabetes have no effect on disease outcome in COVID-19 patients[33] whereas other studies have found that hypertension and diabetes, with or without obesity, are independently associated with a poor outcome .[34]

A study of nearly 4000 critically ill patients with COVID-19 hospitalized in intensive care has shown that hypertension, diabetes, cardiovascular disease, hypercholesterolemia, chronic kidney disease, and other comorbidities were predictive of mortality. However, of these comorbidities, only diabetes and hypercholesterolemia were independent predictors.[35] A study of only hypertensive patients has reported that diabetes was not an independent prognostic factor, whereas age and chronic kidney disease were independent predictors. This study has found that diabetes, hypertension, and obesity were independent predictors of severe COVID-19 regardless of patients' sex; the strongest predictor in patients younger than 50 years old was obesity, whereas no association was found between age and either hypertension or diabetes.[36] However, the authors did not adjust for all comorbidities as in the first mentioned study of the same patient cohort.

The National Cohort Study in England studied 19 256 ICU admissions related to COVID-19 and found that patients with type 2 diabetes had an increased risk of mortality independent of hypertension, chronic respiratory disease, chronic heart disease, chronic kidney disease, chronic liver disease, or other potential risk factors.[37]Another study has shown no association between hypertension and mortality or acute respiratory distress syndrome (ARDS) in patients with COVID-19.[32] The authors have shown that either hypertension or diabetes, individually or in comorbidity, was an independent predictor of ARDS and mortality in patients with COVID-19.[3] Gupta and coworkers have revealed that only body mass index $\geq$ 40 kg/m^2 and coronary artery disease were independent predictors of 28-day mortality in COVID-19 patients.[16] Hypertension, diabetes, heart failure, and chronic

obstructive pulmonary disease were not independently associated with mortality in these patients.[33–38]

5 | LIMITATIONS

The results of this meta-analysis should be interpreted with caution. First, the observational and retrospective nature of the selected individual studies limited our ability to draw causal inferences. Therefore, our results may be affected by reverse causality bias or other unknown confounders that were not adjusted for in these studies. Second, individual studies did not provide data on the use of antihypertensive medications, duration of hypertension, and systolic and diastolic blood pressure. Third, only seven studies met our inclusion criteria. A larger prospective study is needed to confirm our results. Despite these limitations, our study has important strengths. We performed extensive database searches to ensure that all relevant and published studies were identified. We did not find heterogeneity among the selected individual studies.

6 | CONCLUSIONS

We found an increased risk of COVID-19 mortality among hypertensive patients in sub-Saharan Africa. Hypertension could be one of the potential predictive variables for COVID-19 mortality that Sub-Saharan hospitals should look for during triage. To minimize in-hospital mortality in COVID-19, patients with a history of hypertension should strictly follow COVID-19 preventive measures and social distancing and be prioritized for COVID-19 vaccination initiatives in sub-Saharan Africa.

ACKNOWLEDGMENT

We thank Siobhan Johnstone for having read the first version of the manuscript.

AUTHOR CONTRIBUTIONS

The study was conceived and designed by B.B. The literature searches and data extraction were carried out by B.B. and O.O. The first draft was written by B.B., H.S., M.S., and J.N. B.B. conducted the analysis. The final text was co-authored by all authors, who double-checked for essential intellectual substance. The text was approved by all authors in its current form.

DATA AVAILABILITY STATEMENT

The data sets reside with the authors of the original papers evaluated.

ORCID

Ben Bepouka MD, MSc https://orcid.org/0000-0003-3063-4234

REFERENCES

1. COVID-19 (WHO African region). Available at: https://who.maps.arcgis.com/apps/dashboards/0c9b3a8b68d0437a8cf28581e9c063a9. Accessed: July 22nd, 2021
2. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: Summary of a report of 72314 cases from the Chinese center for disease control and prevention. *JAMA*. 2020;323:1239-1242.
3. Rodriguez-Iturbe B, Pons H, Johnson RJ. Role of the immunesystem in hypertension. *Physiol Rev*. 2017;97:1127-1164.
4. Guo T, Fan Y, Chen M, et al. Cardiovascular implications of fatal outcomes ofpatients with Coronavirus disease 2019 (COVID-19). *JAMA Cardiol*. 2020;e201017.
5. Guan WJ, Liang WH, Zhao Y, Liang HR, Chen ZS, Li YM. Comorbidity and its impact on 1590 patients withCovid-19 in China: A nationwide analysis. *Eur Respir J*. 2020;55:2000547.6.
6. Chen T, Wu D, Chen H, et al. Clinical characteristics of 113 deceased patients withcoronavirus disease 2019: retrospective study. *Brit Med J*. 2020;368:m1091.
7. Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of coronavirus disease 2019in China. *New Engl J Med*. 2020;382:1708-1720.
8. Li B, Yang J, Zhao F, et al. Prevalence and impact of cardiovascular metabolic diseases on COVID-19 in China. *Clin Res Cardiol*. 2020;109(5):531-538.
9. Parveen R, Sehar N, Bajpai R, Agarwal NB. Association of diabetes and hypertension with disease severity in covid-19 patients: A systematic literature review and exploratory meta-analysis. *Diabetes Res Clin Pract*. 2020;108295.
10. Ssentongo AE, Ssentongo P, Heilbrunn ES, et al. Renin-angiotensin-aldosterone system inhibitors and the risk of mortality in patients with hypertension hospitalised for COVID-19: systematic review and meta-analysis. *Open Heart*. 2020;7(2):e001353.
11. Zhang J, Wu J, Sun X, et al. Association of hypertension with the severity and fatality of SARS-CoV-2 infection: A meta-analysis. *Epidemiol Infect*. 2020;148:e106.
12. Du Y, Zhou N, Zha W, Lv Y. Hypertension is a clinically important risk factor for critical illness and mortality in COVID-19: A meta-analysis. *Nutr Metab Cardiovasc Dis*. 2021;31(3):745-755.
13. Dai XC, An ZY, Wang ZY, Wang ZZ, Wang YR. Associations between the use of renin-angiotensin system inhibitors and the risks of severe COVID-19 and mortality in COVID-19 patients with hypertension: a meta-analysis of observational studies. *Front Cardiovasc Med*. 2021;8:609857.
14. 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.
15. Osibogun A, Balogun M, Abayomi A, et al. Outcomes of COVID-19 patients with comorbidities in southwest Nigeria. *PLoS One*. 2021;16(3):e0248281.
16. Tigist WL, Kindalem GA, Ishmael SH, et al. COVID-19 disease severity and associated factors among ethiopian patients: a study of the millennium COVID-19 care center. *medRxiv*. 2021. https://doi.org/10.1101/2020.10.09.20209999
17. Boulle A, Davies MA, Hussey H, et al. Risk factors for coronavirus disease 2019 (COVID-19) death in a population cohort study from the western cape province, South Africa. *Clin Infect Dis*. 2021;73(7):e2005-e2015. https://doi.org/10.1093/cid/ciaa1198
18. 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.
19. Jaspard M, Sow MS, Juchet S, et al. Clinical presentation, outcomes and factors associated with mortality: a prospective study from three COVID-19 referral care centres in West Africa. *Int J Infect Dis*. 2021;108:45-52.
20. 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.

21. Ghada OH, Maysoun AAY, Doaa SIM. Prediction of COVID-19 mortality among hospitalized patients in Sudan. *MedRxiv*. 2021. https://doi.org/10.1101/2021.03.09.21253179
22. Abraham NS, Byrne CJ, Young JM, Solomon MJ. Meta-analysis of well-designed non randomized comparative studies of surgical procedures is as good as random-ized controlled trials. *J Clin Epidemiol*. 2010;63:238-245.
23. Slim K, Nini E, Forestier D, Kwiatkowski F, Panis Y, Chipponi J. Methodological index for non-randomized studies (MINORS): development and validation of a new instrument. *ANZ J Surg*. 2003;73(9):712-716.
24. Higgins JP, Thompson SG, Deeks JJ, et al. Measuring inconsistency in meta-analyses. *BMJ*. 2003;327:557e560.
25. Viechtbauer W, Cheung MW. Outlier and influence diagnostics for meta-analysis. *Res Synth Methods*. 2010;1:112e125.
26. Yang G, Tan Z, Zhou L, et al. Effects of Angiotensin II Receptor Blockers and ACE (Angiotensin-Converting Enzyme) Inhibitors on Virus Infection, Inflammatory Status, and Clinical Outcomes in Patients With COVID-19 and Hypertension: A Single-Center Retrospective Study. *Hypertension*. 2020;76(1):51-58.
27. Ma RCW, Holt RIG. COVID-19 and diabetes. *Diabet Med*. 2020;37(5):723-725. https://doi.org/10.1111/dme.14300.
28. Pal R, Bhansali A. COVID-19, diabetes mellitus and ACE2: the conundrum. *Diabetes Res Clin Pract*. 2020;108132.
29. Rabelo LA, Alenina N, Bader M. ACE2-angiotensin-(1- 7)-Mas axis and oxidative stress in cardiovascular disease. *Hypertens Res*. 2011;34:154-160.
30. Cohall DH, Scantlebury-Manning T, James S, et al. Reninangiotensin-aldosterone system gender differences in an Afro-Caribbean population. *JRAAS*. 2015;16:539-546.
31. AlGhatrif M, Cingolani O, Lakatta EG. The dilemma of coronavirus disease 2019, aging, and cardiovascular disease: insights from cardiovascular aging science. *JAMA Cardiol*. 2020;5(7):747-748. https://doi.org/10.1001/jamacardio.2020.1329
32. Sun Y, Guan X, Jia L, et al. Independent and combined effects of hypertension and diabetes on clinical outcomes in patients with COVID-19: A retrospective cohort study of Huoshen Mountain Hospital and Guanggu Fangcang Shelter Hospital. *J Clin Hypertens*. 2021;23(2):218-231. https://doi.org/10.1111/jch.14146
33. Gupta S, Hayek SS, Wang W, et al. Factors associated with death in critically ill patients with coronavirus disease 2019 in the US. *JAMA Intern Med*. 2020 180:1–12.
34. Giannouchos TV, Sussman RA, Mier JM, Poulas K, Farsalinos K. Characteristics and risk factors for COVID-19 diagnosis and adverse outcomes in Mexico: an analysis of 89,756 laboratory-confirmed COVID-19 cases. *Eur Respir J*. 2020;30:2002144.
35. Grasselli G, Greco M, Zanella A, et al. Risk factors associated with mortality among patients with COVID-19 in intensive care units in Lombardy, Italy. *JAMA Intern Med*. 2020; 180:1345–55.
36. Denova-Gutiérrez E, Lopez-Gatell H, Alomia-Zegarra JL, et al. The association of obesity, type 2 diabetes, and hypertension with severe coronavirus disease 2019 on Admission among Mexican patients. *Obesity*. 2020;28:1826-1832.
37. Dennis JM, Mateen BA, Sonabend R, et al. Type 2 diabetes and COVID-19-related mortality in the critical care setting: a national cohort study in England, march-july (2020). *Diab Care*. 2020;23: dc201444.
38. Tadic M, Saeed S, Grassi G, Taddei S, Mancia G, Cuspidi C. Hypertension and COVID-19: ongoing controversies. *Front Cardiovasc Med*. 2021;8:639222.

How to cite this article: 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;24:99–105. https://doi.org/10.1111/jch.14417