The burden and outcomes of COVID-19 among patients with co-morbid disease in Africa: protocol for a systematic review and meta-analysis

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Abstract

The coronavirus disease 2019 (COVID-19) outbreak is now a global public health concern and has had an enormous adverse impact in both developed and developing countries. In Africa, in August 2020, the total number of confirmed cases was 1 022 401 cases, with 704 704 recovered and 22 501 deaths. People with co-morbidities are at increased risk of complications and COVID-19-related death. Evidence on the burden and outcome among patients with co-morbid diseases has not been published in Africa, so this systematic review and meta-analysis aims to quantify these. Observational studies reporting on the burden and outcome of COVD-19 among patients with co-morbid diseases in Africa will be included and a search of online databases PubMed/MEDLINE, EMBASE, HINARI, Cochrane Library, World Health Organization COVID-19 database, Africa Wide Knowledge and Web of Science will be applied. Two independent authors will carry out data extraction and assess the risk of bias using a predetermined and structured method of data collection. Disagreements will be resolved by discussion after mutual consensus with a third reviewer who is an experienced researcher (AH) in meta-analysis studies. We will use random-effects to estimate the overall burden and outcome of COVID-19 among patients with co-morbid diseases in Africa. To assess possible publication bias, funnel plot test and Egger's test methods will be used. This systematic review and meta-analysis protocol will be reported based on the Preferred Reporting Items for Systematic reviews and Meta-Analysis protocol guidelines. Results will be stratified by the African geographic region, diagnostic methods and co-morbidity. COVID-19 distribution data will be shown by interest variables such as residence/geographic region, diagnostic methods, type of co-morbidity and outcomes of co-morbidity. The findings of this review will notify health-care professionals about the burden and outcome of COVID-19 among patients with co-morbid diseases while providing evidence to bring about the requisite improvements in clinical practice for these patients.
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Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first identified in Wuhan, Hubei province, China in December 2019. Coronaviruses are a large class of viruses with low pathogenicity and high transmissibility [1,2]. It rapidly became an outbreak and a major global public health concern. WHO has called the outbreak of coronavirus disease 2019 (COVID-19) a global emergency [3].

According to the latest reports, the clinical manifestations of COVID-19 are heterogeneous. The clinical symptoms of COVID-19 vary from asymptomatic illness to flu-like disease, including high morbidity and mortality from multi-organ failure. Most patients diagnosed with COVID-19 develop mild symptoms including dry cough, fever and sore throat, and their disease resolves spontaneously; however, some patients develop multiple complications, such as organ failure, septic shock and pneumonia [4–10].

COVID-19 has contributed to an enormous adverse impact globally. According to the European Centre for Disease

Prevention and Control, on 8 August 2020, the reported cases of COVID-19 were 19 357 085 cases worldwide, with 721 174 deaths. The USA had the largest number of confirmed cases, 4 941 796 with 161 356 deaths, in the world. In Africa, the total number of confirmed cases was 1 022 401 cases, with 704 704 recovered and 22 501 deaths. South Africa has the largest number of reported cases (545 476) in Africa. The five African countries reporting most deaths are South Africa (9909), Egypt (4971), Algeria (1282), Nigeria (936) and Sudan (769) [11,12].

Studies have reported that the presence of any co-morbidity has been associated with increased risk of developing COVID-19 and poorer clinical outcomes than those without co-morbidity [13,14]. From admitted patients, 20%−51% of patients reported having at least one co-morbidity, with diabetes (10%−20%), hypertension (10%−15%) and other cardiovascular and cerebrovascular diseases (7%−40%). People with related co-morbidities are at increased risk of complications and COVID-19-related death [9,13,15,16].

Despite reports about COVID-19, there are no pooled results on the burden and outcomes of COVID-19 among patients with co-morbid diseases in Africa. This research protocol will therefore be designed to conduct a systematic review and meta-analysis of the burden and outcomes of COVID-19 among patients with co-morbid diseases in Africa.

Materials and methods

Protocol registration
This review is registered in the PROSPERO International Prospective Registry of Systematic Reviews (CRD42020202229) and reported according to Preferred Reporting Items for Systematic reviews and Meta-Analysis protocol (PRISMA-P) guidelines [17] (Table 1).

Eligibility criteria
Types of study. All observational studies; including cross-sectional studies, cohort, case−control and baseline results from randomized controlled trials carried out in Africa will be included.

Participants/population. All patients with co-morbid diseases, who live in Africa and have laboratory-confirmed and/or clinically diagnosed COVID-19.

Intervention(s), exposure(s). Patients with co-morbid diseases and COVID-19 infection. Disease severity, mortality, burden and outcome of COVID-19 in patients with co-morbid diseases will be assessed.

Outcomes. Burden and other clinical outcomes of COVID-19 among patients with co-morbid diseases, such as, prevalence rate, infection rate and outcomes of co-morbidity (recovery, complications and death).

Settings. Hospital-based studies.

Language. The articles included in this study will be those articles published only in the English language. This is because of the feasibility associated with reading and understanding other languages.

Method of diagnosis. No limitation on diagnostic methods will be set, but subgroup review will be carried out based on diagnostic instruments. Interim guidance from the WHO and/or any diagnostic criteria proposed by the WHO such as the *WHO interim guidance for laboratory biosafety related to 2019-nCoV* [18,19] will be considered (Table 2).

Exclusion criteria. Observational studies including case reports and case series are excluded. Studies not performed in humans, qualitative studies, studies that lack the relevant data needed to compute the burden and outcome levels of COVID-19 among patients with co-morbid diseases will be excluded from this review.

Quality assessment of included studies
The methodological quality of the included studies will be evaluated using the Newcastle−Ottawa Scale, which was designed to assess the quality of non-randomized studies in meta-analyses. This scale is primarily formulated by a star allocation system, assigning a maximum of ten stars for the risk of bias in three areas: a selection of study groups (four or five stars), comparability of groups (two stars) and ascertainment of the outcome of interest or the exposure (three stars). No validation study provides a cut-off score for rating low-quality studies; a priori, we arbitrarily established that zero to three, four to six and seven to ten stars would be considered as at high, moderate and low risk of bias, respectively [25].

Search strategy and data source
We will search articles reporting the outcome of COVD-19 among patients with co-morbid disease from online databases (PubMed/MEDLINE, Google Scholar, EMBASE, HINARI, Cochrane Library, WHO COVID-19 database, Africa Wide Knowledge and Web of Science) (Table 3) using the following search terms: 'Wuhan coronavirus' OR 'COVID-19' OR 'novel coronavirus' OR '2019-nCoV' OR 'Coronavirus outbreak' OR 'SARS-CoV-2' OR 'SARS2' OR 'Severe acute respiratory syndrome coronavirus 2# OR 'comorbid disease' OR 'non-communicable disease' OR 'chronic disease' OR 'Outcome'.

TABLE 1. PRISMA-P 2015 checklist: recommended items to address in a systematic review protocol

Section/topic	Item no.	Checklist item	Information reported		
			Yes	No	Line number(s)
Administrative Information					
Title					
Identification	1a	Identify the report as a protocol of a systematic review	☐	☐	
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	☐	☐	
Registration	2	If registered, provide the name of the registry (e.g. PROSPERO) and registration number in the Abstract	☐	☐	
Authors					
Contact	3a	Provide name, institutional affiliation and e-mail address of all protocol authors; provide physical mailing address of corresponding author	☐	☐	
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	☐	☐	
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	☐	☐	
Support					
Sources	5a	Indicate sources of financial or other support for the review	☐	☐	
Sponsor	5b	Provide name for the review funder and/or sponsor	☐	☐	
Role of sponsor/funder	5c	Describe roles of funder(s), sponsor(s),and/or institution(s), if any, in developing the protocol	☐	☐	
Introduction					
Rationale	6	Describe the rationale for the review in the context of what is already known	☐	☐	
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators and outcomes (PICO)	☐	☐	
Methods					
Eligibility criteria	8	Specify the study characteristics (e.g. PICO, study design, setting, time frame) and report characteristics (e.g. years considered, language, publication status) to be used as criteria for eligibility for the review	☐	☐	
Information sources	9	Describe all intended information sources (e.g. electronic databases, contact with study authors, trial registers, or other grey literature sources) with planned dates of coverage	☐	☐	
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	☐	☐	
Study records					
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	☐	☐	
Selection process	11b	State the process that will be used for selecting studies (e.g. two independent reviewers) through each phase of the review (i.e. screening, eligibility and inclusion in meta-analysis)	☐	☐	
Data collection process	11c	Describe planned method of extracting data from reports (e.g. piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	☐	☐	
Data items	12	List and define all variables for which data will be sought (e.g. PICO items, funding sources), any pre-planned data assumptions and simplifications	☐	☐	
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	☐	☐	
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	☐	☐	
Data					
Synthesis	15a	Describe criteria under which study data will be quantitatively synthesized	☐	☐	
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (e.g. I^2, Kendall's τ)	☐	☐	
	15c	Describe any proposed additional analyses (e.g. sensitivity or subgroup analyses, meta-regression)	☐	☐	
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	☐	☐	
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (e.g. publication bias across studies, selective reporting within studies)	☐	☐	
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (e.g. GRADE)	☐	☐	

Other search terms will be 'burden' OR 'mortality' OR 'prevalence' OR 'incidence'.

Selection and data collection process

Data will be extracted using a standardized method of data extraction. Two assessors (WA and TM) will autonomously extract data from the included studies using the predefined standardized extraction method. For further consideration of possible inclusion in the study, full texts for the qualifying titles and/or abstracts, including those where there is ambiguity, will be collected. The agreement between the reviewers of the study will be calculated using Cohen's λ statistics. Disagreements will be resolved by discussion after mutual consensus with a third reviewer who is an experienced researcher (AH) in meta-analysis studies. Reasons for excluding articles will be noted.

Where there is missing information, authors will be contacted for more details to check study eligibility. Where necessary, emails will be sent to the corresponding author to request more information before excluding the study. For studies that appear in more than one published article we will consider the most recent, detailed article with the highest sample size. We shall treat each survey as a separate study for

TABLE 2. Laboratory examination of coronavirus disease 2019 in suspected human cases: interim guidance

Test	Type of sample	Timing
Nucleic acid amplification tests (NAAT)	Upper respiratory specimens: nasopharyngeal and oropharyngeal swab nasopharyngeal wash/nasopharyngeal aspirate Lower respiratory specimens: sputum, endotracheal aspirate or bronchoalveolar lavage are preferred for patients with severe respiratory disease	Upon introduction pick. May perform repeated sampling to monitor viral clearance. Additional work is required to assess the efficiency and accuracy of repeat sampling.
Serology and other	Blood and stool are also investigated for coronaviruses	Paired samples are needed to confirm with the original sample obtained during the first week of disease and the second sample preferably obtained after 2−4 weeks (there has to be an ideal timing for convalescent samples)

TABLE 3. Search strategy

Search no.	Databases	No. of articles found	No. of articles included	No. of articles excluded	Reason for exclusion
1	PubMed/MEDLINE	N =	N =	N =	
2	Google Scholar	N =	N =	N =	
3	Cochrane Library	N =	N =	N =	
4	HINARI	N =	N =	N =	
5	EMBASE	N =	N =	N =	
6	WHO COVID-19 database	N =	N =	N =	
7	Africa Wide Knowledge	N =	N =	N =	
8	Web of Science	N =	N =	N =	
9	Unpublished theses, manuscripts and reports from WHO and CDC	N =	N =	N =	

surveys that appear in one article with multiple surveys conducted at different time-points. From each included study, information on the name of the first author, publishing month, country and/or region, complications or outcomes of co-morbidity (recovery, complications and death), diagnostic criteria, type of co-morbidity, COVID-19, study area, prevalence and/or incidence, and characteristics of the study (study design, response rate) will be extracted using a pre-piloted template prepared in a Microsoft excel spreadsheet.

Risk of bias in individual studies
A tool developed by Hoy *et al.* for prevalence studies will be used to evaluate the likelihood of bias and quality of studies included in this review [20]. The tool has 11 items; items 1−4 assess the external validity, 5−10 assess the internal validity and item 11 offers a description of the overall risk by the reviewer based on the responses to the previous ten items, which are rated 1 if yes and 0 if no. Studies are graded as low risk (<3), moderate risk (4−6) or high risk (7−9) of bias. Two reviewers will perform this exercise (KZ, GM), and disputes will be resolved through discussion and, where possible, through arbitration involving a third author. Besides, adequate sampling methods, consistent methods and procedures for collecting data, recorded methods of quality control and representative sample size will be considered as indicators of the study quality. Studies of high quality will be studies that revealed all the points mentioned above (see Supplementary material, Table S1).

Data management
A framework was developed a priori to guide the screening and selection process, based on the inclusion and exclusion criteria. The tool will be piloted and revised before data extraction begins. First, to delete duplicates, the search results will be uploaded to ENDNOTE software. The remaining articles will be put on RAYYAN, a smartphone and web-based software system that facilitates collaboration between the reviewers involved in the screening and selection of studies to be included in the review [20].

Data items
Data extraction will include name of authors, publishing month, country and/or region, sample size, study area, diagnostic criteria, type of co-morbidity, characteristics of the study (study design, response rate), and outcomes of co-morbidity (recovery, complications and death).

Outcomes and prioritization
The primary outcome is the burden and outcome of COVID-19 among patients with co-morbid diseases in Africa.

Data analysis and presentation of results
R software and R STUDIO will be used during analysis. All analyses will be carried out using a 'metaprop' routine for Windows using R version 3.5.3 [21]. Results will be reported as proportions with corresponding 95% CIs. Forest plots will be drawn to represent the combined burden and outcome of
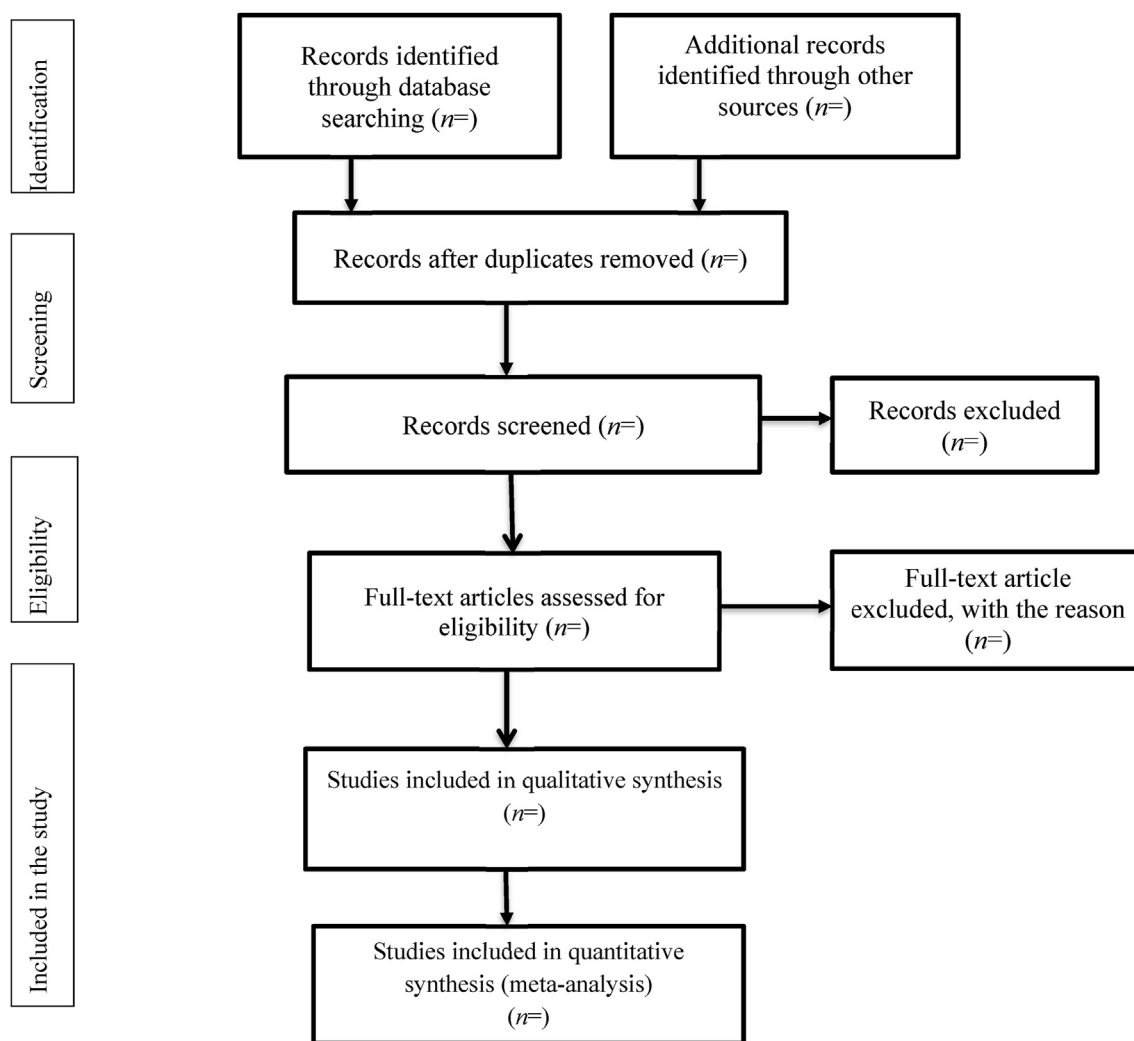
FIG. 1. Flow chart diagram for selection of articles for systemic review and meta-analysis of prevalence and outcome of coronavirus disease 2019 among individuals with diabetes in Africa.

COVID-19 and the extent of statistical heterogeneity among studies. The statistical heterogeneity will be evaluated using the χ^2 test and quantified using calculation of the I^2 statistics with values of 25%, 50% and 75% as representative of low, medium and high heterogeneity, respectively [22]. If there is heterogeneity between studies, we will use a meta-analysis of random-effects [23] to estimate the aggregate burden and outcome of COVID-19 among patients with co-morbid diseases in Africa. To assess possible publication bias, funnel plot test and Egger's test methods will be used [24]. A p value < 0.10 on the Egger's test is considered statistically significant for bias in writing.

Data synthesis

The study-specific burden and outcome of COVID-19 among patients with co-morbidity will be recalculated using crude numerators and denominators from each study. A meta-analysis

will be performed on variables that are similar across the included studies. Because there will be heterogeneity among the studies, a random effect model will be used to determine the burden and outcome of COVID-19 with co-morbidity in Africa. Geographic regions, diagnostic methods and type of co-morbidity will be summarized by a subgroup analysis.

Discussion

This review will be based the PRISMA-P guidelines; the PRISMA flow diagram will be used to document the different phases of the review process [17] (Fig. 1).

The findings of this review will notify health programme planners, decision-makers and health-care professionals about the burden and outcome of COVID-19 among patients with co-

morbidities, while providing evidence to bring about good-quality health care, with emphasis on the problem and on improvements in clinical practice. Conferences, peer-review articles and social media sites will share conclusions from this study.

Conclusion

This systematic review and meta-analysis will be expected to quantify the burden and outcome of COVID-19 among patients with co-morbid diseases in Africa.

Authors' contributions

WA, AH and TM conceived and designed the study. The conceptualization and design were then contributed to by all authors. The initial protocol was drafted by GM, WA KZ, GG, TH and TG. All authors contributed to the development of the selection criteria, the risk of a bias assessment strategy and data extraction criteria. All authors read, provided feedback on and approved the final protocol.

Conflict of interest

The authors declare no competing interests.

Funding

Not applicable.

Availability of data and materials

This study has not been submitted and considered for publication in any journal. The data sets used and/or analyses during the study will be presented within the manuscript and available from the corresponding author on request.

Systematic review registration

This review is registered in the PROSPERO International Prospective Register of Systematic reviews with the registration number of CRD42020202229.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.nmni.2020.100802.

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