Comorbidities, clinical symptoms and complications in severe and non-severe COVID-19 patients: a systematic review and meta-analysis

Review question

What are the comorbidities, clinical symptoms and complications in severe and non-severe COVID-19 patients?

Searches

We will search PubMed, Web of Science, the Cochrane Library, CBM (the Chinese Biomedical Literature Database), CNKI (China National Knowledge Infrastructure), the Wanfang, and the VIP databases.

We will include papers from December 2019.

The search will be limited to the English and Chinese languages.

The search terms will be used as follows: “Wuhan coronavirus” OR “COVID-19” OR “novel coronavirus” OR “2019-nCoV” OR “coronavirus disease” OR “SARS-CoV-2” OR “SARS2” OR “severe acute respiratory syndrome coronavirus 2”.

We will also hand search the reference lists of included papers, and will contact experts in the field to ensure a comprehensive review.

Additional search strategy information can be found in the attached PDF document (link provided below).

Types of study to be included

Inclusion:

1. Studies which have examined laboratory-confirmed patients with COVID-19. (any age or COVID-19 subtype);

2. Studies which have examined the demographic (e.g. age, gender), early comorbidities (e.g. diabetes, hypertension etc.), clinical symptoms (e.g. fever, cough, etc.), complications (e.g. acute respiratory distress syndrome, acute kidney injury, etc.), and outcomes (e.g. hospitalization, discharge, etc.) of severe and (or) non-severe patients with COVID-19;

3. Studies reporting mean ± SDs or proportion and 95% confidence interval (95% CI) of these factors;

4. Observational studies will be included.

Exclusion:

1. Studies which do not contribute to any factors of this study. (i.e. if the samples have been included in a general way, there could be serious risk of duplication, as the samples of many of the eligible articles have been investigated from the same hospital);

2. Studies which do not provide a full-text version;

3. Studies not published in either English or Chinese.

Condition or domain being studied

COVID-19 is a zoonotic virus that can lead to secondary human infections, and is closely related (with 88% identity) to two bat-derived severe acute respiratory syndrome (SARS)-like coronaviruses, bat-SL-CoVZC45 and bat-SL-CoVZXC21, but which is more distant from SARS-CoV (about 79%) and MERS-CoV (about 50%), and is new, appearing in December 2019.

This pathogen can cause severe respiratory conditions, requiring specialized management at intensive care units (ICU), although the differences in comorbidities, clinical symptoms and complications between severe and non-severe COVID-19 patients are currently unknown.

We aim, therefore, to compare the demographic features, comorbidities, clinical symptoms, complications and outcomes between these two groups, to further clarify the aspects of this new infection, and to help healthcare workers make decisions regarding treatment.

Participants/population

Patients who have been laboratory-confirmed as having COVID-19, according to WHO guidance.

Intervention(s), exposure(s)

Comorbidities, clinical symptoms and complications in severe and non-severe COVID-19 patients.

All demographic factors (e.g. age, gender), early comorbidities (e.g. diabetes, hypertension etc.), clinical symptoms (e.g. fever, cough, etc.), complications (e.g. acute respiratory distress syndrome (ARDS), acute kidney injury (AKI), etc.), and outcomes (e.g. hospitalization, discharge, etc.) data will be reviewed.

Comparator(s)/control

Severity (severe/ICU vs non-severe/non-ICU), and geographic region (Wuhan, China vs outside Wuhan).

Context

Main outcome(s)

The pooled proportion or mean and 95% confidence interval (95% CI) data of demographics (e.g. age, gender), early comorbidities (e.g. diabetes, hypertension etc.), clinical symptoms (e.g. fever, cough, etc.), complications (e.g. acute respiratory distress syndrome, acute kidney injury, etc.), and outcomes (e.g. hospitalization, discharge, etc.).

Establishment of the differences between severe and non-severe COVID-19 patients for the above mentioned factors.

* Measures of effect

Quantitative data will be measured as the number of occurrences of an event versus the total number of people reported for that event (n/N).

Additionally, we will use the mean and standard deviation (SD), or median and interquartile range (IQR) (or median and range), to record the measurement data.
Unit discordance for variables will be resolved by converting all units to a standard measurement for that variable.

We will use a random-effects model, or a fixed-effect model, to calculate the pooled proportion or mean and 95% confidence interval (95% CI) of all reported variables.

All P values will be based on two-sided tests and be considered statistically significant at P<0.05.

Additional outcome(s)

None.

* Measures of effect

Not applicable.

Data extraction (selection and coding)

After excluding duplicate papers, one researcher (WZ) will then screen the titles and abstracts of the studies retrieved during the searches against the eligibility criteria.

Then two researchers (DH, OC) will assess full texts of those articles identified as being relevant for eligibility.

The Kappa value for study selection between the researchers will be tested, and consensus on the inclusion of all studies will be agreed by two researchers (DH, OC), with any disagreements being resolved in discussion with a third researcher (WZ).

Data will then be extracted from the studies selected for inclusion.

Two researchers will complete standardized data extracted forms independently, and a third researcher will check the extracted data to ensure that there are no mistakes or duplicated information.

Where available, the following information from each article will be extracted: title, study design, study period, location, first author, publication year, sample size (e.g. total size, severe size, non-severe size), sex distribution, any comorbidities (e.g. diabetes, hypertension, cardiovascular disease, COPD, malignancy, chronic liver disease), clinical symptoms (e.g. fever, cough, myalgia or fatigue, sputum production), complications (e.g. ARDS, acute kidney injury, shock), outcomes (e.g. hospitalization, discharge, death). Discrepancies will be resolved by discussion with a third investigator.

We will extract the quantitative data as the number of occurrences of an event versus the total number of people reported for that event (n/N).

Additionally, we will use the mean and standard deviation (SD), or median and interquartile range (IQR) (or median and range), to record the measurement data.

Risk of bias (quality) assessment

Two researchers (OC, DH) will assess the risk of bias of the individual included papers using the Newcastle-Ottawa Scale (NOS) for assessing the quality of cohort studies and case-control studies. This tool considers the domains of selection, comparability, and the ascertainment of the outcome of interest.

A study with a score of 0-3, 4-6 and 7-9 will be considered as being of poor, intermediate and high quality, respectively.

The weighted Kappa value will be used to test the quality rating criteria, and consensus will be achieved through discussion in the event of any disagreements between the researchers regarding individual ratings.

Strategy for data synthesis

We will synthesize the included data, even if only two papers are identified for inclusion, although data synthesized from more than ten papers will be mainly discussed.

Quantitative data will be measured as the number of occurrences of an event versus the total number of people reported for that event (n/N).

Additionally, we will use the mean and standard deviation (SD), or median and interquartile range (IQR) (or median and range), to record the measurement data. Unit discordance for variables will be resolved by converting all units to a standard measurement for that variable.
All analyses will be conducted using R software Version 3.6.1 (http://CRAN.R-project.org, R Foundation, Vienna, Austria).
We will mainly conduct the analyses by severity (severe vs non-severe).

We will use a random-effects model or a fixed-effects model to calculate the pooled proportion or mean and 95% confidence interval (95% CI) of all reported variables.

All P values will be based on two-sided tests, and will be considered to be statistically significant at P<0.05.

Measure of heterogeneity, including Cochran's Q statistic, the I^2 index and the $?^2$ test, will be estimated and reported.

Pooled results from the random-effects model will be reported when the I^2 >50% and P (heterogeneity)<0.10, which indicates substantial levels of heterogeneity.

Publication bias will be checked by the visual inspection of funnel plots, and tested using Egger’s test if ten or more studies report a particular variable, and the Egger test, with P<0.05, will be considered to be an indication of substantial publication bias.

Analysis of subgroups or subsets
We will conduct subgroup analyses based on severity (severe/ICU vs non-severe/non-ICU) and geographic region (Wuhan, China vs outside of Wuhan).

Type and method of review
Epidemiologic, Meta-analysis, Prevention, Systematic review

Anticipated or actual start date
29 February 2020

Anticipated completion date
01 July 2020

Funding sources/sponsors
None

Conflicts of interest

Language
English

Country
China

Stage of review
Review Ongoing

Subject index terms status
Subject indexing assigned by CRD

Subject index terms
Comorbidity; Coronavirus; Coronavirus Infections; Disease Progression; Humans; Public Health; Risk; Risk Factors; Signs and Symptoms, Respiratory; Treatment Outcome

Date of registration in PROSPERO
08 April 2020

Date of publication of this version
08 April 2020

Details of any existing review of the same topic by the same authors

Stage of review at time of this submission
The review has not started

Stage	Started	Completed
Preliminary searches	No	No
Piloting of the study selection process	No	No
Formal screening of search results against eligibility criteria	No	No
Data extraction	No	No
Risk of bias (quality) assessment	No	No
Data analysis	No	No

The record owner confirms that the information they have supplied for this submission is accurate and complete and they understand that deliberate provision of inaccurate information or omission of data may be construed as scientific misconduct.

The record owner confirms that they will update the status of the review when it is completed and will add publication details in due course.

Versions
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