Prevalence of Depression, Anxiety, Delirium, and Post-traumatic Stress Disorder Among COVID-19 Patients: Protocol for a Living Systematic Review

Jiyuan Shi
lanzhou university
Liang Zhao
Lanzhou University
Yuanyuan Li
Lanzhou University
Meili Yan
Lanzhou University
Niu Mingming
Lanzhou University
Yamin Chen
Lanzhou University
Ziwei Song
Lanzhou University
Ya Gao
Lanzhou University
Ruixing Zhang
zhengzhou university
Jinhui Tian (15038059737@163.com)
Evidence-Based Nursing Centre, School of nursing, Lanzhou University, Lanzhou City 730000, Gansu Province, China. 2School of Basic Medical Sciences, Lanzhou University, Lanzhou City, 730000, Gansu Province, China.

Protocol

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Abstract

Background

Previous studies on the impact of COVID-19 on the mental health of the patients has been limited by the lack of relevant data. With the rapid and sustained growth of the publications on COVID-19 research, we will perform a living systematic review (LSR) to provide comprehensive and continuously updated data to explore the prevalence of depression, anxiety, delirium, and post-traumatic stress disorder (PTSD) among COVID-19 patients.

Methods

We will perform a comprehensive search of the following databases: Cochrane library, PubMed, Web of Science, Embase, and Chinese Biomedicine Literature to identify relevant studies. We will utilize different tools to examine the bias risks (quality) regarding studies of varying design types, such as the Newcastle-Ottawa Scale (NOS) for cohort and case-control studies, etc. Study inclusion, data extraction, and risk of bias assessments will be performed independently by two reviewers. The literature searches would be updated every three months. We will perform meta-analysis if any new eligible studies or data are obtained and resubmit an updated systematic review if any change in outcomes and heterogeneity is determined after the addition of the new studies.

Discussion

This LSR would provide an in-depth and up-to-date summary of the psychological impact of COVID-19 diagnosis and treatment on the patients.

Systematic review registration

PROSPERO CRD42020196610

Background

The global outbreak of the COVID-19 has been designated as a pandemic that has affected more than ten million people, with more than half a million fatalities [1, 2]. Previous research focusing on pandemics confirmed that individuals who had experienced public health emergencies reported varying degrees of psychological disorders even after the event ended or they were cured and discharged from the hospital [3–6]. Patients with confirmed and suspected infections may suffer from repeated psychiatric and neuropsychiatric incidences due to multiple reasons, such as progression of the disease, adverse drug reaction, social isolation, uncertainty, and physical discomfort [7–9].

A recently published systematic review and meta-analysis indicated the incidence of delirium as a common occurrence amongst patients hospitalized due to severe coronavirus infections (SARS-CoV and MERS-CoV), whereas, PTSD, anxiety, depression, and fatigue were observed in the subsequent months [3].

There exists some preliminary/unpublished data showing psychiatric and neuropsychiatric presentations in COVID-19 patients [3]. Since the spread of COVID-19, there has been extensive research on the topic globally, translating into an unprecedented number of publications, approximately 59 articles per day, probably higher than observed for any other disease [10]. It is essential to collect continuously updated data to provide convincing evidence for patients, healthcare workers, and policymakers. A living systematic review (LSR) retains the benefits of a systematic review and accepts continual updating of the relevant data without compromising the methodological rigor [11–14].

The aim of this study is to provide a living systematic review for synthesizing rapid and continual updating of data on whether the common neuropsychiatric conditions observed in patients hospitalized for severe SARS-CoV or MERS-CoV are also prevalent in a different stage of COVID-19 patients.

Methods/design

Study design

This systematic review has been designed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) statement and has been registered on PROSPERO (CRD42020196610) [15]

Eligibility criteria

Population

Included are: (1) COVID-19 infection patients among adults (≥18 years of age) who are diagnosed with four types of psychiatric and neuropsychiatric syndromes (anxiety (e.g. generalized anxiety, panic attack), depression, delirium, and post-traumatic stress disorder), with no age, gender or setting, location or ethnicity restrictions. (2) psychiatric and neuropsychiatric syndromes diagnosed by a trained researcher or health professional according to the criterion defined by ICD-10, ICD-11, DSM-IV, DSM-V, and Chinese Classification of Mental Disorders - 3 (CCMD-3) or by validated psychometric scales (e.g, clinician—administered PTSD scale for PTSD) with established cutoffs approved by psychologists (RXZ). (3) studies published in English and Chinese.

Excluded are: (1) studies explored the indirect effects of SARS-CoV-2 on the mental health of family members, care providers, or isolated people who did not infect. (2) populations with other coronavirus diseases (severe acute respiratory syndrome (SARS) or Middle East respiratory syndrome (MERS) unless the trial authors provided subgroup data for people with COVID-19). (3) studies in which patients self-reported as anxiety, depression, delirium, and post-traumatic stress disorder, or studies that did not report symptom measurement methods or diagnostic criteria. (4) patients with a prevalence of psychiatric and neuropsychiatric syndromes reported before a diagnosis of COVID-19.

Type of outcomes

The primary outcomes is the prevalence of depression, anxiety, delirium, and PTSD. Secondary outcomes are the incidence of mortality in COVID-19 patients with depression, anxiety, delirium or PTSD, the measurement of health-related quality of life score using Short Form 12 Health Survey Questionnaire (SF-12), or Short Form 36 Health Survey Questionnaire (SF-36). The outcome will be classified as examining the acute or post-illness psychiatric consequences of infection on the basis of whether information is collected during the patient's illness or the period after the illness.

If a study met our criteria reports on COVID-19 infection that were not specified a priori as outcomes of interest for this review, the results will be noted in a narrative synthesis or reported in the summary of findings table (e.g, symptom severity as defined by different scales), but not necessarily pooled for meta-analyses.

Studies design

We will include only peer-reviewed cohort studies, cross-sectional studies. We will exclude duplicate publications (i.e, two or more studies investigating the same sample). Conference abstracts, commentaries, or opinion pieces will also be excluded because they lack adequate information for meta-analysis.

Search strategy

A senior investigator (Y.G.) would examine the published and gray literature sources to extract the studies reporting the prevalence of depression, PTSD, anxiety, or delirium in COVID-19 patients. An experienced medical information specialist (J.H.T.) would further check and approve the search methodology. We will conduct a comprehensive search of Cochrane library, PubMed, Web of Science, Embase, and Chinese Biomedicine Literature to extract articles/abstracts published between the inception of this disease (1 December 2019) until the completion of this review will be included. There will be no restrictions on language or year of publication. An additional file, which would describe the complete search strategy for PubMed as well as other electronic databases will be provided. We will also thoroughly search the reference lists of the relevant reviews and research trials. We have presented the search strategy using PubMed as an example in Table 1. The search strategy will be adapted to fit other online databases as well.

Update plan

We will perform identical search operations at regular pre-defined intervals to identify newly published data. There are no robust standards for the update frequency based on current research; however, due to the unprecedented number of publications on COVID-19, we will update the literature searches every three months, and perform meta-analysis if any new eligible studies or data are obtained. We will submit an updated systematic review if we observe any changes in the outcomes and heterogeneity after the addition of new studies or provide data on additional outcomes [11, 12]. We chose this updating

frequency to allow quick updates and to highlight the most recent information to the researchers, clinicians, nurses, and policymakers [11, 14, 16].

Study selection

Original literature search records will be imported into Endnote X9 software tool (Thomson Reuters, New York, NY, USA) management software. Two authors (JYS and YG) will independently retrieve full-text of potential studies after deduplication to assess their eligibility according to the abovementioned inclusion criteria. The selection process will be conducted under the supervision of a psychologist (RXZ). Any disagreement will be resolved by the reviewer (JHT).

Data extraction

Two independent reviewers (JYS and MMN) will be involved in data extraction; we will extract country of patients, gender, age, sample size, study design (e.g, cohort studies), diagnostic criteria for the viral infection (such as WHO criteria), criteria for the definition of depression, anxiety, delirium, and PTSD (e.g, ICD-11), population type (e.g, pregnant women), the severity of the symptoms defined by different scales (e.g, clinician—administered PTSD scale for PTSD), number of signs or symptoms (e.g, depression, anxiety), quality of life scores,timing (acute vs post-illness), and length of follow-up.

Risk of bias (quality) assessment.

Two independent reviewers (JYS and YG) will use the following tools to examine the risk of bias in the included studies: the Newcastle-Ottawa Scale (NOS) for cohort studies [17]. The 11-item checklist recommended by the Agency for Healthcare Research and Quality (AHRQ) will be used to assess the quality of the cross-sectional studies include [18]. We will classify the methodological quality of each individual study as having a low, high, or unclear risk of bias as describing in Table 1. Any disagreement regarding inclusion of some studies will be resolved by discussion and consensus between the two reviewers. If this failed, it shall be resolved by the third reviewer (JHT).

Processing missing data

We will contact the corresponding or other primary authors to obtain missing data or insufficiently reported data after selecting the studies. In addition, we will estimate missing data if they can be extracted from tables or figures. Trials with missing data that cannot be obtained will be excluded for reasons. Any significant deviations between the protocol and the final review will be reported clearly.

Data analysis

The Stata (v13.0; StataCorp) and Revman 5 were used for statistical analysis. The statistical heterogeneity will be examined using the Cochran's Q and the I^2 statistic. An $I^2 > 50\%$, and a *p*-value < 0.05 will correspond to significant heterogeneity, and a random-effects model will be used for the subgroup analyses and pooled estimates. On the contrary, an $I^2 < 50\%$ and a *p*-value > 0.05 will correspond to

insignificant heterogeneity, and the fixed-effect model shall be used for the subsequent meta-analysis. We defined point prevalences for the rate of depression, anxiety, delirium, and PTSD diagnoses. The effect size measures were prevalence with 95% CIs (for number of signs or symptoms, quality of life scores) and mean difference with 95% CI (proportion of depression, anxiety, delirium, and PTSD diagnoses; the incidence of mortality). The heterogeneity/publication bias will be examined using the Egger's test or the symmetry of the funnel plot. In the Egger's test, bias will be significant when *p*-value < 0.05.

Subgroup analysis

Provided sufficient data is available, the following subgroup analyses will be planned for main outcomes if data are sufficient: age (< 60 vs. ≥ 60 years), setting (developed countries vs. developing countries), gender (male vs. female), databases (data from Chinese databases vs. data from English databases), and follow-up time.

Sensitivity analyses

We will perform sensitivity analyses to assess the influence of the study 's methodological risk of bias. To do this, we will repeat any meta-analyses by excluding data from studies classified as a high risk of bias.

Quality of the evidence

The Grades of Recommendations, Assessment, Development, and Evaluation (GRADE) Working Group method will be used to examine the quality of the evidence for each outcome. We will assess each outcome based on each of the following five aspects: imprecision, inconsistency, limitations, indirectness, and publication bias. They will be rated as very-low, low, moderate, or high level [19, 20].

Discussion

Coronaviruses have resulted in two severe outbreaks of severe acute respiratory syndrome (SARS); however, before SARS-CoV-2. Previous coronaviruses have been associated with delirium signs in the acute stage and fatigue, depression, PTSD, and anxiety in the post-illness stage [3]. However, the lack of adequate data on COVID-19 patients limited the previous study to investigate and conclude the effects of the SARS-CoV-2 infection on patients' mental health. Given that the rapid and sustained growth of publication of COVID-19 research, we will perform an LSR to comprehensive and continuous synthesis updated data to explore the prevalence of depression, anxiety, delirium, and PTSD in COVID-19 patients.

Abbreviations

LSR
living systematic review
PRISMA-P
Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocol

PTSD
post-traumatic stress disorder
PROSPERO
International Prospective Register of Systematic Reviews
RCT
Randomized controlled trial
GRADE
Grades of Recommendations, Assessment, Development, and Evaluation
SARS
Severe outbreaks of severe acute respiratory syndrome
MERS
Middle East respiratory syndrome

Declarations

Ethics approval and consent to participate

All authors are accountable for all aspects of this work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The present study will not involve any patients and/or the public. No ethical approve or informed consent is required for the purposes of the present study.

Consent for publication

Not applicable.

Availability of data and materials

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

JYS and JHT led the drafting of the manuscript. JYS, LZ and JHT contributed to the design of the systematic review. All authors contributed to the development and final approval of the manuscript.

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Tables

Table2. Risk of bias assessment for included studies.

Study design	Tool	Domains/Checklist	Overall risk of bias judgement
Cross-sectional studies	AHRQ checklist	1. Define the source of information (survey, record review) 2. List inclusion and exclusion criteria for exposed and unexposed subjects (cases and controls) or refer to previous publications 3. Indicate time period used for identifying patients 4. 4Indicate whether or not subjects were consecutive if not population-based 5. Indicate if evaluators of subjective components of study were masked to other aspects of the status of the participants 6. Describe any assessments undertaken for quality assurance purposes (e.g., test/retest of primary outcome measurements) 7. Explain any patient exclusions from analysis 8. Describe how confounding was assessed and/or controlled. 9. If applicable, explain how missing data were handled in the analysis 10. Summarize patient response rates and completeness of data collection 11. Clarify what follow-up, if any, was expected and the percentage of patients for which incomplete data or follow-up was obtained	An item would be scored “0” if it was answered “No” or “Unlear”; if it was answered “Yes”, then the item scored “1”. Article quality was assessed as follows: low quality = 0-3; moderate quality = 4-7; high quality = 8-11.
Cohort studied,	NOS	1. Was selection of exposed and non-exposed cohorts drawn from the same population? 2. Can we be confident in the assessment of exposure? 3. Can we be confident that the outcome of interest was not present at start of study?,	An item would be scored “0” if it was answered “No” or “Unlear”; if it was answered “Yes”, then the item scored “1”. Article quality was assessed as follows: low risk of bias: total score≤ 5; high risk of bias: total score > 5.

	4. Did the statistical analysis adjust for all confounders? 5. Can we be confident in the assessment of the presence or absence of potential confounders? 6. Can we be confident in the assessment of outcome? 7. Was the follow up of cohorts adequate?

RoB: Risk of Bias; ROBINS: Risk of Bias in Non-randomized Studies of Interventions; AHRQ: Agency for Healthcare Research and Quality; NOS: Newcastle Ottawa Scale;

Supplementary Files

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- EDITORIALCERTIFICATE.pdf