Pre-Existing Neurological Conditions and COVID-19 Risk: A Commissioned Rapid Review

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INTRODUCTION

The current outbreak of the novel coronavirus disease (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has spread and infected patients worldwide. Most patients infected exhibit mild to moderate symptoms, but those who exhibit a severe reaction develop severe pneumonia that can progress to acute respiratory distress syndrome (ARDS), septic shock, and/or multiple organ failure. Pre-existing conditions have been considered risk factors for severe COVID-19 and death. The aim of this rapid review is to investigate the impact of pre-existing neurological disease on the clinical course and outcome of COVID-19.

MATERIALS& METHODS

In February 2021, the World Health Organization (WHO) commissioned a rapid review of literature to investigate the impact of pre-existing neurological disease on the clinical course and outcome of COVID-19.

Search strategy and selection criteria

The PubMed database and the WHO COVID-19 database, a curated database of all published articles on COVID-19, were used to search for and identify articles that could be used for this rapid review. The search terms used were “2019 novel coronavirus”, “2019 nCOV”, “COVID-19”, “SARS-CoV-2”, “comorbidity”, “pre-existing”, “Neurological”, “Brain”, “CNS”, “dementia”, “epilepsy”, “stroke”, “intracranial”, “multiple sclerosis”, “Parkinson disease”, “movement disorder”, “autism”, “MIS-C”, “cerebral palsy”, “demyelinating”, “demyelination”, “GBS”, “brain tumor”, “motor neuron disease”, “ALS”, “myasthenia gravis”, ”myopathy”, “myositis”, ”risk”, “morbidity”, “association”, “correlation”, “severity”, “hospitalization”, “death”, and “dying”, with additional shortcuts added to the searches in the WHO COVID-19 database. There was no language restriction applied to the search, and the results from the two searches were screened for duplicates which were removed from the final list of articles to be screened.

Eligibility criteria

Diagnosis of COVID-19 was defined as a positive reverse transcription polymerase chain reaction (RT PCR) for SARS-CoV-2 or strong clinical and radiological suspicion of COVID-19 diagnosis. Pre-existing neurological conditions were defined as any chronic disease of the nervous system shown to have had onset prior to the diagnosis of COVID-19.

Inclusion criteria:

- Studies were included if they investigated the impact of pre-existing neurological disease on the course of COVID-19
- Studies were included if they investigated the role of pre-existing neurological diseases as a risk factor for death in COVID-19 patients
- Studies that investigated both pre-existing neurological and non-neurological diseases were included in the review, but only findings pertaining to pre-existing neurological conditions were included in the analysis
- Cohort studies, retrospective analyses, case-control studies, case series, systematic reviews, and meta-analyses published between 1st January 2020 and 4th April 2021 were included

Exclusion criteria:

- Studies were excluded if they did not investigate any pre-existing neurological diseases in COVID-19 patients
- Single case reports were excluded
- Non-systematic reviews were excluded
- Letters to editors were excluded

Data analysis

Odds ratios (OR) from cohort, retrospective, case series, and case-control studies for associations between pre-existing neurological disease and severe COVID-19 and/or death were noted and pooled ORs were calculated using Stata version 13.0. Studies that did not include odds ratios were not included in the analysis.

Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) criteria were applied to evaluate the quality of the evidence reported by the studies using mortality and severity of COVID-19 as the outcomes. Authors reviewed at least two of the articles and made judgements on risk of bias, indirectness, and imprecision of the articles based on design and methodology in each study. The outcomes of each study were summarized using effect size measurements. The inconsistency among studies and certainty of evidence were also judged for each outcome based on study design.

RESULTS

Twenty-six articles from 12 countries across three continents with a total of 379,947 COVID-19 patients was included. The most common pre-existing neurological conditions investigated in the studies were stroke or cerebrovascular disease (15/26 studies) and dementia (11/26 studies). Other pre-existing neurological diseases included were Parkinson’s disease, epilepsy, multiple sclerosis, and neurological tumors (Figure 2).

Association with severe COVID-19 and mortality

The mean age of the 379,947 COVID-19 patients was 57 years (SD 10.93), 51.3% of whom were female. Pre-existing neurological disease, particularly cerebrovascular disease and dementia, was shown to be a risk factor for severe COVID-19 with a pooled OR of 1.99 (1.81 – 2.18). There was also an increased risk of death with a pooled OR for pre-existing neurological disease overall 1.74 (1.56–1.94).

GRADE evidence profile

Risk of bias was judge to be high in majority of studies resulting from inherent bias arising from study design used and inclusion of only hospitalized patients that likely biased the findings towards more severe COVID-19 illness. *Imprecision* was judged to be moderate to high due to inclusion of multiple comorbidities by some studies. *Inconsistency* was low-to-moderate as finding were similar overall throughout the studies included.

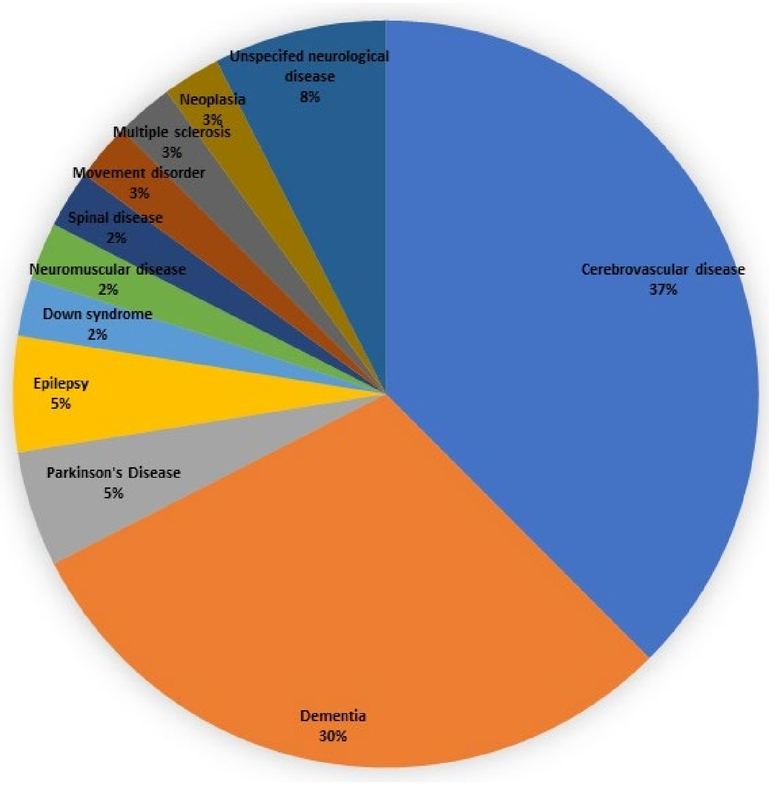

Figure 2

DISCUSSION & CONCLUSION

This review of 26 studies showed that pre-existing cerebrovascular disease and pre-existing dementia are risk factors for severe COVID-19 and/or death.

The limitations of this rapid review include the use of only two databases which may have limited the scope of the searches. The generalizability of the findings is also challenging as not only were certain regions such as South America, Australia, and Africa unrepresented, but the findings also did not inform on pediatric populations.

The findings suggest that pre-existing neurological disease is a significant risk factor for severe COVID-19 and mortality. However, further investigation to consolidate these findings are required through large multi-national cohort studies.

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Presented at the 97th Annual Session of the Greater New York Dental Meeting in 2021