Temporal association between COVID-19 infection and subsequent new-onset dementia in older adults (aged 60 years and above): a systematic review and meta-analysis

Authorship

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Abstract

Background: The association between COVID-19 and the risk of new-onset dementia (NOD) in older adults remains poorly understood. We aimed to quantify the approximate risk of NOD following COVID-19 infection in this population, considering various follow-up periods and control groups.

Methods: In this systematic review and meta-analysis, we searched MEDLINE/PubMed, PsycINFO, Scopus and medRxiv for English studies published from January 2020 to December 2023, focusing exclusively on original research investigating the link between COVID-19 infection and NOD. We primarily assessed the risk of developing NOD over time among older adults aged 60 and above after infection, using Risk Ratio (RR) for measurement. Included study quality was assessed using the nine-star Newcastle–Ottawa Scale (NOS). Control groups were categorized as: (i) a non-COVID cohort with other respiratory infections (control group[C1]); and (ii) a non-COVID cohort with otherwise unspecified health status (control group[C2]). Follow-up periods ranged from 3 to 24 months post-COVID. This study adheres to PRISMA guidelines and is registered with PROSPERO (CRD42023491714).

Findings: We identified 11 studies involving 939,824 post-COVID-19 survivors and 6,765,117 controls that were eligible for analysis. The average quality appraisal NOS score was 8.5 (SD=0.66), indicating a generally high methodological quality of the included studies. Across a median observation period of 12 months post-COVID, the overall incidence of NOD was 1.82% in the COVID-infected group, compared to 0.35% in the non-COVID-infected group. The overall pooled meta-analysis showed a significantly increased NOD risk among COVID-19 older adult survivors compared to non-COVID-19 controls (i.e., C1 and C2 grouped together;

RR=1.58, 95%CI 1.21–2.08). Similar increased NOD risks were observed in subgroup analyses restricted to an observational period of 12 months (1.56, 1.21–2.01), as well as in 5 studies that employed Propensity Score Matching to sufficiently and effectively control for multiple confounding covariates (1.46, 1.10-1.94). This risk was more heightened when specifically compared to C2 group at 12 months post-COVID-19 (1.84, 1.41–2.38). Nevertheless, COVID-19 group and C1 group exhibited a similarly increased risk of developing NOD (1.13, 0.92–1.38). Additionally, female gender and severe COVID-19 infection were associated with significantly higher NOD risks. Heterogeneity varied across different outcomes (I^2=0–98%).

Interpretation: We mainly found that COVID-19 may be associated with a significantly increased risk of developing NOD in older adults, a risk similar to that posed by other respiratory infections. However, the need for extended observation periods to reach more definitive conclusions presents a notable limitation. Although the integrated results from PSM studies, which largely ensured comparability of baseline characteristics between COVID-positive and control groups, provided more robust evidence, there remains a potential for residual confounding factors. Given the irreversible nature and profound impacts of dementia on individuals, families, and society, our preliminary evidence highlights the need for continuous cognitive health monitoring in older adults recovering from COVID-19. This may inform healthcare strategies to mitigate long-term cognitive decline in this vulnerable population in the UK.

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Contributors

DS, TC, and CH conceived the idea of the review. DS, CXYW, TC, and CH designed the review methodology. DS and CXYW did the search and screened the articles. DS completed the meta-analysis and wrote the first draft of the abstract. CXYW, TC and CH revised the abstract. All authors critically reviewed and approved the abstract.

Declaration of interests

We declare no competing interests.