

Review article

Impact of COVID-19 on functional, cognitive, neuropsychiatric, and health-related outcomes in patients with dementia: A systematic review

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ARTICLE INFO

Keywords:

Mild cognitive impairment
Dementia
Mortality rate
SARS-CoV-2
COVID-19
functioning

ABSTRACT

Background: This systematic review analyzes the impact of COVID-19 on dementia patients' functional, cognitive, neuropsychiatric, and health related outcomes. It hypothesizes that dementia patients infected with SARS-CoV-2 experience more pronounced deterioration compared to those who are uninfected.

Methods: Research from 01/03/2020 to 07/10/2023 was conducted using Medline, Web of Science, and Embase databases, and adhering to PRISMA guidelines and the PICO framework. The study aimed to determine if SARS-CoV-2 infection is associated with worse outcomes in dementia patients. The protocol is registered in PROSPERO (CRD42022352481), and bias was evaluated using the Newcastle-Ottawa Scale.

Results: Among 198 studies reviewed, only three met the criteria. Chen et al. (2023) identified higher mortality in SARS-CoV-2-infected dementia patients, while Merla et al. (2023) observed faster cognitive decline in infected individuals with increased hospital admissions. Additionally, Cascini et al. (2022) reported an increased risk of infection and significantly elevated mortality in dementia patients, highlighting comorbidities and antipsychotic medication use as key risk factors.

Conclusion: These limited data suggest higher mortality and cognitive decline in dementia patients following COVID-19, underscoring the need for extensive research in this area.

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1. Introduction

In 2020, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) rapidly spread across the globe. Clinical manifestations of coronavirus disease 2019 (COVID-19) exhibit a broad spectrum, from mild to severe. Various studies have highlighted an array of sequels, some linked to the initial clinical presentation severity [1,2], while others were unrelated [3].

In 2023, the World Health Organization (WHO) estimated a general COVID-19 mortality rate of approximately 0.70% (WHO, 2023). Several risk factors, including advanced age, male sex, pre-existing comorbidities, pre-existing neurological diseases [4]; immunization status, racial/ethnic disparities in healthcare access, prior exposure to SARS-CoV-2, and occupation as a healthcare worker, increase the risk of severe disease and mortality [5]. Some factors, such as older age, inherently pose a greater risk due to weakened immune responses, heightened prevalence of comorbidities [6], and aging-related chronic pro-inflammatory immune states [7].

Despite numerous studies on COVID-19's cognitive impacts, targeted research on individuals with pre-existing cognitive impairment still needs to be made available [8]. It is vital to discern COVID-19's repercussions on this population, as they may confront distinct challenges, accelerated cognitive decline, and exacerbated health outcomes.

Individuals with cognitive impairment, especially those with dementia, have an increased vulnerability to upper respiratory infections, both viral (e.g., influenza) and bacterial (e.g., community-acquired pneumonia) [9,10]. This susceptibility, theorized to result from impaired personal hygiene and self-care stemming from cognitive decline, influences short- and long-term mortality rates [11,12]. Significant post-infection cognitive decline has been observed, lasting up to six months [13]. Therefore, studying COVID-19's impact on those with antecedent cognitive impairments—covering cognitive and neuropsychiatric outcomes, along with mortality risk—is critical.

Although COVID-19 is no longer considered a Public Health Emergency of International Concern (PHEIC), according to WHO, it still poses profound global health implications. Given the potential for its indefinite presence and mutation propensity, proactive measures, such as the WHO-Europe's transition plan for COVID-19, are essential. It is equally crucial to persistently study COVID-19's effects on patients with dementia, providing insights to tailor treatment and care strategies. Hence, health systems should brace for this enduring and unpredictable adversary. Sustained research endeavors, informed by the pandemic's lessons, are needed to aptly address future health crises and dementia patients' specific concerns.

While there have been preliminary investigations into the longitudinal outcomes of patients with MCI and dementia about COVID-19 infection, a thorough examination of the available data has not been conducted. This systematic review aims to assess the existing evidence on the cognitive and functional decline in patients with MCI and dementia, contrasting those who contracted SARS-CoV-2 with those who remained uninfected.

2. Materials and methods

The study protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO: registration number CRD42022352481). This systematic review was reported following the Preferred Reporting Items for Systematic Reviews (PRISMA) recommendations [14]. This systematic review was developed by the WHO's Neurology and COVID-19 Global Forum working group. The interdisciplinary group includes experts from four continents and comprises neurologists, geriatricians, neuropsychologists, psychiatrists, and epidemiologists.

2.1. Eligibility criteria

The PICO (Population, Intervention/issue of interest, Comparison, and Outcome) question was formulated as follows: "In patients with dementia, is there an association between SARS-CoV-2 infection and worse health-related outcomes (including functional, cognitive, and neuropsychiatric) compared to patients of equivalent dementia severity who remained uninfected?" The study population includes patients with previous medical diagnoses of dementia (mild to severe). The intervention/exposure includes being infected with SARS-CoV-2 (confirmed by real-time polymerase chain reaction (RT-PCR) test / nasopharyngeal swabs). The comparison group consists of patients with the same dementia severity as the patient group but without SARS-CoV-2 infection. Outcomes included functional, cognitive, neuropsychiatric, and health-related measures (during the acute phase of COVID-19 and after recovery).

2.2. Search strategy

A systematic literature search was performed in December 2023 in Medline, Web of Science, and Embase. The systematic literature review's literature search and study selection process included articles published between 01/03/2020 and 07/10/2023. The Supplementary material presents the search strategies (see Appendix A).

2.3. Study inclusion and exclusion criteria

The inclusion criteria were as follows: a) articles with patients with all types of dementia who had SARS-CoV-2 infection or not, b) published as of 2020, c) with reported outcomes and d) original reports such as case-control or cohort studies. The exclusion criteria were a) duplicate articles, b) unrelated ones, c) systematic reviews, d) case series with less than 5 cases, and 6) abstracts only. There were no restrictions regarding the study's language.

Two reviewers (LC, GK) independently screened the titles and abstracts according to the eligibility criteria. Disagreements were discussed with a third reviewer (IC) and resolved via consensus (see Fig. 1).

2.4. Data extraction and synthesis

The following data categories were collected when available: study design, sample size, country, patient demographics, population setting, time of assessment related to SARS-CoV-2 infection, comorbidity, outcome measures, and COVID-19 disease severity. One of the reviewers performed the data extraction, and the other reviewer assessed the accuracy of the extracted data (see Table 1).

2.5. Risk of bias assessment

Two reviewers independently rated the quality of included studies using the Newcastle-Ottawa Scale (NOS) (see Table 2). The quality of case-control and cohort studies was assessed by judging three categories: the selection of the study groups, the comparability of the groups, and the ascertainment of either the exposure or outcome of interest for case-control or cohort studies, respectively.

3. Results

3.1. Overview of the included studies

3.1.1. Study selection

After removing the duplicates, 1,670 records were identified from the databases (see Fig. 1). Screening titles and abstracts excluded a total of 1,472 studies. Other studies were also left out after reading the full text because their aims were unrelated ($n = 186$) to those selected for this review.

3.1.2. Study characteristics

The remaining 12 studies are described in Table 1; only 3 of them fully matched the PICO criteria and were included. The remaining studied also aimed to investigate the impact of COVID-19 on patients with dementia but were excluded as they did not meet the complete PICO requirements as they did not include a comparison group (control group); this is why they are discussed as supplementary studies [15–23].

3.2. Results of individual studies

Only three studies met the eligibility criteria [24–26]. Chen [25] and Merla [26], explore different outcomes related to dementia patients with and without SARS-CoV-2 infection. Chen [25] focused on mortality risk, Merla [26] examined cognitive decline and hospitalization rates, while Cascini [24] investigated the broader effects of the pandemic on infection risk and mortality in a large cohort of dementia patients.

Chen's [25] retrospective study evaluated the longer-term effects of SARS-CoV-2 infection in 165 dementia patients who survived COVID-19 during their hospital admission, comparing them to 1325 dementia patients hospitalized without contracting the virus. The analysis included socio-demographic data, clinical variables, and other relevant factors. Chen [25] found that dementia patients with a history of SARS-CoV-2 infection exhibited a significantly higher risk of death, with an adjusted hazard ratio (aHR) of 4.44 (95 % CI 3.13–6.30), which persisted for up to 125 days post-recovery. Clinical factors commonly associated with increased COVID-19 mortality—such as inflammation, hypernatremia, liver dysfunction, and hypoalbuminemia—were also

predictors of mortality in these patients. Moreover, dementia patients who were prescribed antipsychotics (aHR = 3.06, 95 % CI 1.40–6.69) or benzodiazepines (aHR = 3.00, 95 % CI 1.28–7.03) had an elevated risk of death. Based on these findings, Chen [25] developed a predictive model with 87.2 % accuracy for post-acute COVID-19 mortality in dementia patients during the first 120 days post-recovery, offering potential guidance for targeted follow-up and interventions.

Merla [26] focused on cognitive outcomes and functional decline in 31 dementia patients who contracted SARS-CoV-2, compared to 80 uninfected dementia patients. The study found that cognitive decline, defined as a five-point loss on the Mini-Mental State Examination (MMSE), was more prevalent in the COVID-19 group (weighted hazard ratio 3.56, 95 % CI 1.50–8.59, $p = 0.004$). Although the average annual MMSE decline was 1.7 points across both groups, the COVID-19 group experienced a significantly faster rate of decline (3.3 points/year vs. 1.7 points/year, $p < 0.050$). Functional decline in basic and instrumental activities of daily living (BADL and IADL) occurred at similar rates between the two groups, decreasing by less than 1 point/year on average. However, Merla [26] also reported a significantly higher rate of new institutionalizations among COVID-19 patients (45 % vs. 20 %, $p = 0.016$).

Cascini [24] further explored the pandemic's effects on a larger cohort of 31,201 dementia patients aged ≥ 65 using administrative databases linked to the SARS-CoV-2 infection surveillance system. Approximately 7 % of these patients contracted COVID-19, and the analysis revealed a 60 % increased risk of infection and significantly elevated mortality (31.0 per 100; 95 % CI: 28.8–33.6) in the infected

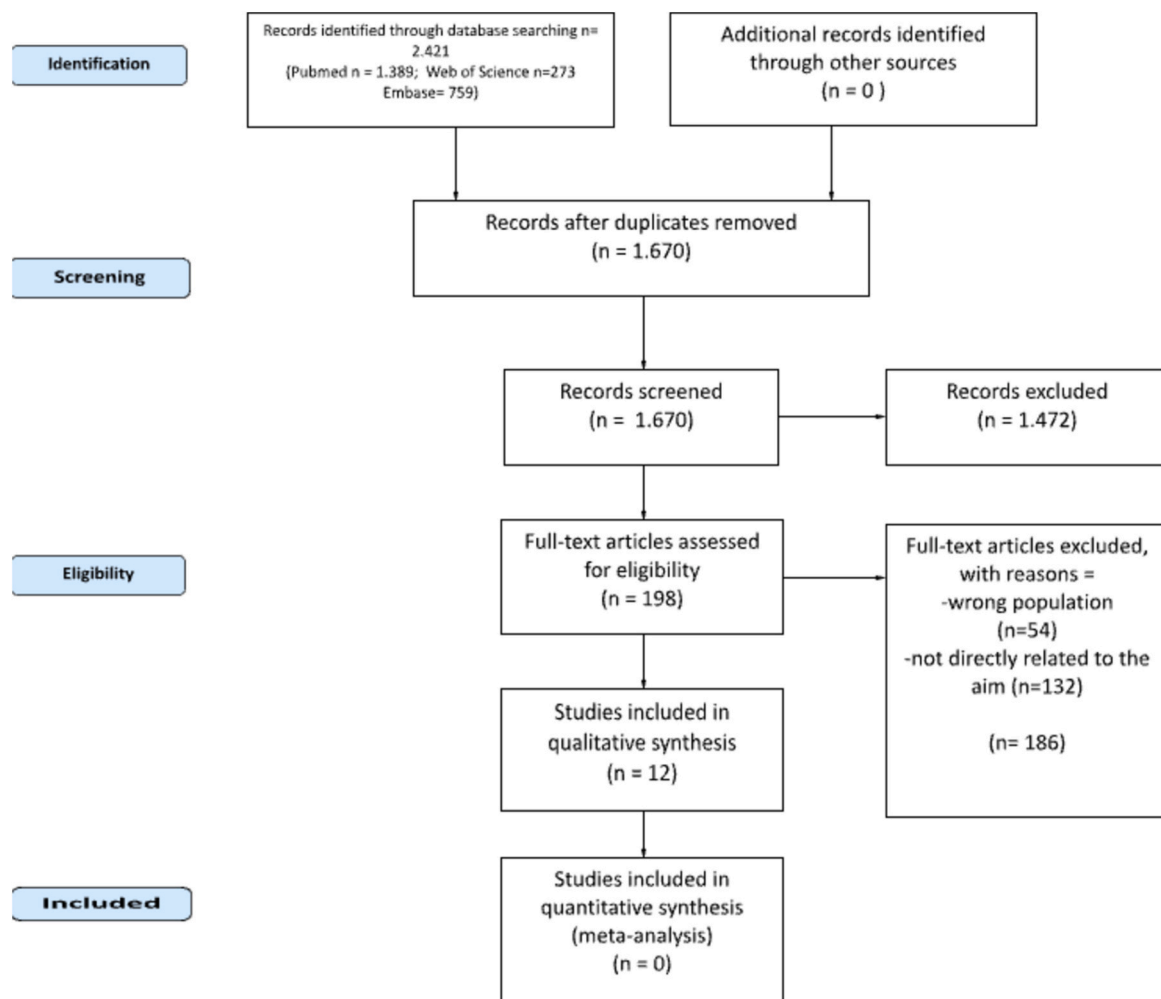


Fig. 1. PRISMA flow chart describing the screening and selection of articles.

Table 1
Characteristics of the included studies: methodological summary and main results.*

Authors	Country	Population setting	COVID-19 cases	Age	Sex (F%)	Diagnosis	Co-morbidity	Dementia severity	Time of Assessment	Control group	Age	Sex (F %)	Dementia severity	Measures	Results	Reasons for Exclusion
COHORT																
Lozano Montoya et al., 2021 ¹⁵	Spain	Acute Geriatric Unit	134 Hospitalized	86.3 (6.6)*	62.7*	45.1 % patients had dementia of some degree	CCI	GDS 0-3: 164 (55.2); GDS 4: 35 (11.8), GDS 5: 38 (12.8), GDS 6: 42 (14.1), GDS 7: 18 (6.1), GDS Dementia >4: 134 (45.1)	24 hs	NA	NA	NA	NA	BI, GDS, CAM, CFS, CCI	Patients with dementia exhibited an increased risk of mortality compared to non-dementia patients. The factors were independently associated with higher in-hospital mortality: a CURB-65 score of 3-5 (HR 7.99, 95 % CI 3.55-19.96, $p < 0.001$), incident delirium (HR 1.72, 95 % CI 1.10-2.70, $p = 0.017$), and a diagnosis of dementia (HR 3.01, 95 % CI 1.37-6.705, $p = 0.017$).	Lack of a control group
Cascini et al., 2022 ²⁴	Italy	Regional Health Assistance file and the Integrated Surveillance System of SARS-CoV-2 infections	2548 Hospitalized	65-74 (12.7 %) 75-84 (44.7 %) >85 (42.9 %)	69.9	Dementia diagnosis identified by health administrative databases.	Cardiovascular comorbidities, diabetes, obesity, COPD, asthma, pneumonia, neoplasm, electrolytes, chronic kidney, gastric diseases, Parkinson's, disease of the blood, chronic liver, fracture, anxiety, alcohol use disorder, depression	NA	14 months	35,181	≥ 65 Years	65.2	NA	SIR and SMR ratios were calculated.	COVID-19- was associated with a crude case fatality rate of 31 %, with a more than double risk of dying in dementia patients compared to the general population of the same age and gender. The SMRs 2.32 (95 % CI 2.05-2.65) for men, and 2.82 (95 % CI 2.55-3.11) for women.	Included
Lucijanic et al., 2022 ¹⁶	Croatia	Registry project-Dubrava University Hospital	357 Mild, moderate, severe and critical	70, IQR (60-80) *	44.1*	N/A	CCI	NA	4 months	NA	NA	NA	NA	CCI	In a multivariate analysis, independent predictors of post-discharge mortality included age > 75, ECOG status, white blood cell count >7/L, red cell distribution width > 14 %, admission urea >10.5 mmol/L, mechanical ventilation,	Lack control group

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Table 1 (continued)

Authors	Country	Population setting	COVID-19 cases	Age	Sex (F%)	Diagnosis	Co-morbidity	Dementia severity	Time of Assessment	Control group	Age	Sex (F %)	Dementia severity	Measures	Results	Reasons for Exclusion
Covino et al., 2020 ¹⁷	Italy	Urban teaching hospital	8 Mild, severe and critical	84 (82–89) *	46.4*	Severe dementia	BP, CAD, CHF, COPD, GCS, ICU, NEWS, pO ₂ , HBP, cerebrovascular disease, diabetes, dementia, malignancy, pneumonia	NA	1 month	NA	NA	NA	NA	Physiological parameters, Symptoms at admission, Radiographic findings, Patient disease presentation in ED, Clinical history	readmission, absence of obesity, COPD, dementia , and metastatic malignancy (P < 0.05 for all). Severe dementia , oxygen levels (pO ₂) of 90 or below upon admission, and lactate dehydrogenase levels exceeding 464 U/L are independent factors that affect survival in these patients. Significant predictors for mortality included comorbidities such as solid organ transplant (p < 0.001), dementia (p < 0.001), chronic kidney disease (p < 0.001), severe mental illness (p < 0.001), diabetes (p < 0.001), chronic obstructive pulmonary disease (COPD) (p < 0.001), cancer (p < 0.001), HBP (p < 0.001).	Lack control group
Ge et al., 2021 ¹⁸	Canada	Ontario Laboratories Information System (OLIS)	8.610 Hospitalized	42.7 (21.9)*	52*	N/A	HBP, asthma, diabetes, HIV, chronic kidney disease, cancer, COPD, rheumatoid arthritis, inflammatory bowel disease, liver disease, severe mental illness and solid organ transplant	NA	1 month	NA	NA	NA	NA	Cases were linked to health administrative databases maintained in the ICES	Significant predictors for mortality included comorbidities such as solid organ transplant (p < 0.001), dementia (p < 0.001), chronic kidney disease (p < 0.001), severe mental illness (p < 0.001), diabetes (p < 0.001), chronic obstructive pulmonary disease (COPD) (p < 0.001), cancer (p < 0.001), HBP (p < 0.001).	Lack of a control group
Vlachogiannis et al., 2022 ¹⁹	UK	Hospital	471 Hospitalized	74 (25)	47.3	N/A	CCI with the addition of obesity, respiratory rate, oxygen saturation on room air, Glasgow Coma Scale score, urea, and C-reactive protein	NA	271 (14) days	NA	NA	NA	NA	Signs and symptoms, laboratory features, co-morbidities, 4C mortality and CFS	Respiratory failure, systemic inflammation, and renal impairment were associated with early mortality, while active cancer and dementia were associated with late mortality.	Lack control group
Hu et al., 2022 ²⁰	UK	UK Biobank	2617 Asymptomatic and mild	74.2 (5.84)	53.6	ICD-10 and ICD-9 (2014 primary neurodegenerative diseases, 345 vascular neurodegenerative diseases, 904 other	CCI	NA	18 months	93,658 (97.3 %) included in the unexposed group	67.7	NA	NA	Demographical factors, lifestyle, socioeconomic status, BMI, Charlson Index	Among individuals with a positive test result for SARS-CoV-2, individuals with neurodegenerative diseases had a higher risk of COVID-19 related death than	Lack of a control group

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Table 1 (continued)

Authors	Country	Population setting	COVID-19 cases	Age	Sex (F%)	Diagnosis	Co-morbidity	Dementia severity	Time of Assessment	Control group	Age	Sex (F %)	Dementia severity	Measures	Results	Reasons for Exclusion
Merla et al., 2023 ²⁶	Italy	Memory Care Facility of the Department of Continuity of Care in Trieste	31 Moderate and hospitalized	83 ± 5	64	neurodegenerative diseases) AD: 7 Vascular dementia: 6 Mixed: 13 Other: 5	Hypertension, diabetes, dyslipidemia, cerebrovascular disease, cardiovascular disease, chronic kidney disease	NA	1.1 year [0.7–1.7]	80	82 ± 5	70	NA	MMSE, BADL and IADL	others (fully adjusted odds ratio 2.08; 95 % CI 1.71–2.53). Cognitive decline was 3.5 times more frequent in COVID-19 patients (HR 3.56, 95 % CI 1.50–8.59, $p = 0.004$). The MMSE score decreased by 1.7 points/year on average, but this decline doubled in COVID-19 patients (3.3 vs. 1.7 points/year, $p < 0.05$). There was a significant increase in fatigue ($p = 0.001$) and depression ($p = 0.016$) scores following COVID-19. The mean Frontal Assessment Battery ($p < 0.001$) and Addenbrooke's Cognitive Examination ($p = 0.001$) scores also significantly worsened.	Included
Dubey et al., 2023 ²¹	India	Burdwan Medical College and Hospital, Bangur Institute of Neurosciences, and private cognitive specialty clinics	14 Hospitalized	65.6 ± 5.02	36	AD: 4 PD: 3 FTD: 2 Vascular dementia: 5	Cardiovascular disease	NA	1 year	NA	NA	NA	NA	ACE-III, FAB, Trail Making Test Part B, CDR, Patient Health Questionnaire and MRI	The mean Frontal Assessment Battery ($p < 0.001$) and Addenbrooke's Cognitive Examination ($p = 0.001$) scores also significantly worsened.	Lack of a control group
CASE CONTROL Beobide Telleria et al., 2022 ²²	Spain	Residents that lived in NHs	116 Hospitalized	85.68 (8.6)	71.7	57: GDS ≥ 6	BMI, AHT, COPD, Dementia; Diabetes	GDS ≥ 6	NA	181	85.53 (8.8)	72,6	GDS ≥ 6	BMI, GDS, Frail VIG	People with dementia and GDS ≥ 6 had a lower likelihood of SARS-CoV-2 infection (OR 0.64, 95 % CI 0.43–0.97, $p < 0.05$). Advanced dementia (GDS ≥ 6), COPD, and antipsychotic use were linked to higher COVID-19 mortality, with both a low Barthel Index and advanced dementia associated with increased mortality risk ($p < 0.05$). Abnormalities on investigation associated with	Lack control group
Chen et al., 2023 ²⁵	UK	Cambridge University Hospitals	165 Moderate and severe	85.6 (7.4)	58,8	ICD-10	CCI	NA	239.4 and 363.8 days	1325	85.2 (7.1)	59,8	NA	Socio-demographic variables, CCI,	Abnormalities on investigation associated with	Included

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Table 1 (continued)

Authors	Country	Population setting	COVID-19 cases	Age	Sex (F%)	Diagnosis	Co-morbidity	Dementia severity	Time of Assessment	Control group	Age	Sex (F %)	Dementia severity	Measures	Results	Reasons for Exclusion
CASE SERIES Matias-Guiu et al., 2020 ²³		(CUH) National Health Service (NHS) Foundation Trust												medicine utilization at baseline, laboratory blood results	increased mortality included high white cell count (aHR = 1.21, 95 %CI 1.04–1.39), higher absolute neutrophil count (aHR = 1.28, 95 %CI 1.12–1.46), higher C-reactive protein (aHR = 1.01, 95 %CI 1.00–1.02), higher serum sodium (aHR = 1.09, 95 % CI 1.01–1.19), and higher ionized calcium (aHR = 1.03, 95 %CI 1.00–1.06).	
	Spain	Tertiary hospital	204 Hospitalized	78.02 (9.42)	58.3	146 (72.1 %) with AD and 57 (27.9 %) with FTD	HBP	CDR, 16.7 % classified as very mild, 27.9 % mild, 28.4 % moderate, and 27.0 % as severe dementia.	NA	NA	NA	NA	NA	A semi-structural interview was conducted to the principal caregivers and included the following items: diagnosis of COVID-19 (RT-PCR) or serological test; symptoms of COVID-19; the need of hospital admission.	Death was associated with older age (83.92 ± 6.76 versus 77.59 ± 9.48, $t = 2.77$, $p = 0.015$) and with an advanced clinical dementia stage ($\chi^2 = 8.58$, $p = 0.035$). No statistically significant differences in the frequency of infection between patients with AD (22, 15.1 %) and FTD (8, 14.8 %) ($\chi^2 = 0.002$, $p = 0.964$). Patients with AD showed a higher risk of death in COVID-19 than patients with FTD.	Lack control group

Reference of the table: Alzheimer’s Disease (DA), Parkinson’s Disease (PD), Frontotemporal Dementia (FTD), Hazard Ratio (HR), The Charlson Comorbidity Index (CCI), Institute for Clinical Evaluative Sciences (ICES), Body Mass Index (BMI); Hypertension (AHT), High Blood Pressure (HBP), Chronic Obstructive Pulmonary disease (COPD), Human Immunodeficiency Virus (HIV), Blood pressure (BP), Coronary Artery Disease (CAD), Congestive heart failure (CHF), Glasgow Coma Scale (GCS), Intensive Care Unit (ICU), National Early Warning Score (NEWS), Peripheral Oxygen Saturation (pO2), Clinical Dementia Rating (CDR), Global Deterioration Scale (GDS), Barthel Index (BI), Confusion Assessment Method (CAM), Age-standardized incidence (SIR) and mortality (SMR), Frailty Index based on the Comprehensive Geriatric Assessment (Frail VIG), Coronavirus Clinical Characterisation Consortium (4C) mortality and Clinical Frailty Scale (CFS), Emergency Department (ED), International Classification of Diseases codes (ICD-10 and ICD-9), Basal Activity of Daily Living (BADL), Mini-Mental State Examination (MMSE), Instrumental Activity of Daily Living (IADL), Addenbrooke’s Cognitive Examination III (ACE-III), Frontal Assessment Battery (FAB), Trail Making Test Part B (TMT B), Patient Health Questionnaire (PHQ), Brain magnetic resonance (MRI), Eastern Cooperative Oncology Group (ECOG).

* Demographic data corresponding to the full sample of the research.

Table 2

. Study designs and quality scoring using Newcastle-Ottawa scale for non-randomised studies in meta-analyses and classification according to AHRQ standards.

Study	Design	Bias Rating Newcastle Ottawa			AHRQ
		Selection	Comparability	Outcome/ exposure	
Merla., et al. 2023	Cohort	***	**	**	Good
Chen., et al. 2023	Case control	**	**	**	Good
Cascini et al., 2022	Cohort	***	**	**	Good

group. The standardized mortality ratio (SMR) was notably higher for both males (2.32; 95 % CI 2.05–2.65) and females (2.82; 95 % CI 2.55–3.11). Comorbidities and antipsychotic medication use emerged as key risk factors, with symptom severity at diagnosis and male gender contributing to higher COVID-19-related mortality. These findings highlight the importance of careful, individualized monitoring to mitigate risks in dementia patients.

Together, these studies highlight distinct yet complementary risks faced by dementia patients during the COVID-19 pandemic. While Chen [25] underscores the heightened mortality risk in the post-acute phase, Merla [26] emphasizes the accelerated cognitive decline and increased likelihood of institutionalization among those affected by the virus, and Cascini [24] highlights the importance of comorbidities and antipsychotic medication use in determining mortality rates. These findings underscore the need for continued monitoring and tailored interventions for dementia patients in the context of COVID-19 recovery.

3.3. Risk of bias assessment results

In summary, when using the Agency for Health Research and Quality (AHRQ) threshold standards, the three included studies were good (see Table 2).

3.4. Supplementary studies

Several studies partially met the PICO requirements; having a control group was the main reason for exclusion (see “Reasons for Exclusion” in Table 1). However, these studies are still noteworthy for discussion as they present COVID-19-related outcomes in patients with dementia.

In this regard, the study of Dubey [21] followed 14 patients with different types of (Alzheimer’s disease, vascular dementia, Parkinson’s disease dementia, and the behavioral variant of frontotemporal dementia) before and one year after SARS-CoV-2 infection. Regardless of dementia subtype, the severity of COVID-19, the presence of vascular risk factors, or the need for oxygen or ventilator support, patients exhibited marked cognitive decline, increased periventricular white matter hyperintensities, and global cortical atrophy. This suggests that COVID-19 may accelerate neurodegeneration, primarily affecting subcortical cognitive functions and contributing to the onset or worsening of white matter lesions.

Beobide Telleria [22], in a case-control study, examined risk factors for COVID-19 infection and mortality among 436 elderly residents. They found that advanced dementia was associated with a reduced infection risk (OR = 0.65; 95 % CI 0.43–0.97), while COPD (OR = 7.8; 95 % CI 1.9–31.3) and antipsychotic medication use (OR = 3.1; 95 % CI 1.0–9.0) were significantly associated with higher mortality. This highlights how the clinical complexity of dementia patients influences their risk profiles during the pandemic.

Along the same lines, Matias-Guiu [23] examined a cohort of dementia patients with Alzheimer’s disease (AD) and frontotemporal dementia (FTD) who were hospitalized due to COVID-19. The frequency of infection was similar between AD (22 cases, 15.1 %) and FTD (8 cases,

14.8 %) patients ($\chi^2 = 0.002, p = 0.964$). Although a diagnosis of AD was associated with higher mortality, this association did not reach statistical significance in the overall sample. However, among those infected with COVID-19, the mortality rate was significantly higher in AD patients (12 out of 22, 54.5 %) compared to FTD patients (1 out of 9, 7.7 %) ($\chi^2 = 4.94, p = 0.045$).

The UK Biobank study by Hu [20] provided further evidence of the increased susceptibility of individuals with pre-existing neurodegenerative diseases. Among 96,275 participants with available SARS-CoV-2 test results, those with a prior diagnosis of neurodegenerative diseases ($n = 2617$) were at increased risk for COVID-19 infection (OR = 2.47; 95 % CI 2.25–2.71), hospitalization (OR = 2.18; 95 % CI 1.94–2.45), and mortality (OR = 3.67; 95 % CI 3.11–4.34). This further underscores the vulnerability of dementia patients to severe COVID-19 outcomes.

In addition to these findings, other studies [15–19] have consistently highlighted the role of dementia as a significant comorbidity in COVID-19 patients. Covino [17] demonstrated that severe dementia independently increased the risk of mortality in COVID-19 patients over 80 years of age. Similarly, Lozano Montoya [15] found a strong association between dementia and in-hospital mortality, with delirium and high Pneumonia Severity Scores contributing to poor outcomes. Lucijanic [16] extended these observations by revealing a significant post-discharge mortality risk in dementia patients, with a hazard ratio of 4.32 (95 % CI 3.23–5.77) over a 12-month follow-up period. Vlachogannis [19] further corroborated these results, showing that dementia was the only comorbidity associated with both early and late mortality. After adjusting for confounders such as age and sex, the increased risk persisted, particularly for late mortality.

Overall, these studies collectively underscore the amplified vulnerability of dementia patients during SARS-CoV-2 infection, not only during hospitalization but also throughout the recovery period. Increased risk of infection, combined with the progression of cognitive decline, severe outcomes, and long-term mortality, highlights the urgent need for tailored care strategies to protect and support this high-risk population during and after the pandemic.

4. Discussion

This review assesses the current literature on the impact of COVID-19 on patients with dementia, particularly focusing on functional, cognitive, neuropsychiatric, and health-related outcomes compared to an appropriate control group. Our extensive search identified only three studies [24–26] that met the eligibility criteria, highlighting a notable gap in research. Although this may be due to the specific nature of our research questions and the restrictive search strategies employed, the results we found are critical and point to an urgent need for further studies with control groups to better understand the effects of SARS-CoV-2 infection in patients with dementia. Notably, the existing research primarily addresses the risk of mortality, with limited exploration of cognitive and neuropsychiatric outcomes.

Our systematic analysis suggests a clear link between dementia and an elevated risk of severe outcomes and mortality from COVID-19 infection. This finding is consistent with other meta-analyses, such as those by Liu [27] and Hariyanto [28], which report that dementia significantly increases the mortality rate in COVID-19 patients. Several factors may explain this increased risk. Chen [25] highlight that dementia patients who contract SARS-CoV-2 face a higher risk of mortality, even after recovery from the acute phase of the disease. This finding aligns with the studies by Cascini [24] and Hu [20], which also report higher mortality rates and a greater susceptibility to infection among individuals with dementia.

The mechanisms underlying this increased vulnerability remain unclear, but one possible explanation involves immune system dysregulation commonly associated with neurodegenerative diseases, which may lead to altered immune responses [29–32]. Chronic inflammation, often present in neurodegenerative conditions, could further increase

the risk of contracting and experiencing severe outcomes from SARS-CoV-2 infection [33,34]. Moreover, dementia patients often have compromised immune systems and suffer from comorbidities such as hypertension, diabetes, and pneumonia, which may contribute to severe COVID-19 outcomes [35]. The interaction between dementia, comorbidities, and COVID-19 outcomes has been explored in several systematic reviews [36], which indicate that dementia patients are at a higher risk for infection, severe outcomes, and mortality. This population is particularly prone to heightened neuroinflammation, potentially worsening the effects of COVID-19 due to pre-existing brain inflammatory neurodegeneration, leading to poorer prognosis [37].

Additionally, certain medications used to manage dementia, particularly antipsychotics and benzodiazepines, may contribute to the greater severity of COVID-19 outcomes. Chen [25] and Beobide Telleria [23] underscore the increased risks posed by these medications, further complicating the management of COVID-19 in dementia patients.

Cognitive decline in dementia patients following COVID-19 infection has been consistently reported in the literature [38]. For instance, Merla [26] emphasizes the significant acceleration of cognitive decline in dementia patients infected with SARS-CoV-2, as evidenced by their MMSE scores. This accelerated cognitive decline not only impacts patients' quality of life but also places additional burdens on healthcare systems and caregivers. Therefore, there is an urgent need for tailored medical and social care strategies to support patients with dementia in the context of SARS-CoV-2 infection.

The strengths of our review lie in its adherence to the PRISMA guidelines and the use of the PICO framework, which enabled the identification of high-quality studies. However, this rigorous approach also meant excluding several studies that, while not meeting all our eligibility criteria, still provide valuable insights into COVID-19's effects on patients with dementia. For example, the UK Biobank study, though not exclusively focused on patients with dementia, compares outcomes with a robust control group and provides a clear indication of increased risk of infection, hospitalization, and mortality among individuals with neurodegenerative diseases [20]. We discussed these supplementary studies in the Results and used their findings to support our primary analysis in this Discussion section.

In summary, the role of dementia as a comorbid condition in the context of SARS-CoV-2 infection has gained significant attention. Several studies identify dementia as a predictor of increased mortality and reveal that even post-discharge, dementia patients have a markedly higher mortality risk. These findings emphasize the need for clinicians to consider dementia as a key factor when managing COVID-19 patients, necessitating specialized care strategies and vigilant post-infection follow-up. Furthermore, our review underscores the urgent need for systematic case-control studies to investigate the cognitive, functional, neuropsychiatric, and health-related outcomes in patients with mild cognitive impairment and dementia after COVID-19 infection.

Although our findings indicate that dementia patients infected with SARS-CoV-2 face higher mortality and worse cognitive outcomes, there remain important research questions. For example, the role of preventive interventions, including vaccination, has been shown to mitigate severe outcomes among older adults with cognitive impairment [39]. Further research is needed to explore proactive care strategies for this high-risk group. Additionally, there is a lack of studies that examine the correlation between the severity of COVID-19 infection and cognitive or functional decline, nor those that follow up with patients beyond one year post-infection.

5. Conclusion

The available literature indicates that dementia patients infected with SARS-CoV-2 face an increased risk of mortality and accelerated cognitive decline compared to those uninfected. Our review, although based on limited evidence, underscores the critical need for further research in this area. The heightened vulnerability of this population

may result from immune system dysregulation, chronic inflammation, comorbidities, and the use of certain medications, such as antipsychotics and benzodiazepines. These findings highlight the need for tailored care strategies and vigilant monitoring of dementia patients, both during and after COVID-19 infection.

Declaration of generative AI

Nothing to report.

Funding

Nothing to report.

Ethical approval and consent to participate

No applicable.

Consent for publication

No applicable.

CRediT authorship contribution statement

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Declaration of competing interest

Nothing to report.

Data availability

Data sharing is not applicable to this article as no data sets were generated or analyzed during the current study.

Acknowledgements

The authors acknowledge the contribution of all the WHO's Neurology and COVID-19 Global Forum working group members on Follow-up and Long-term Impact.

Arianna Fornari is supported by the Italian Ministry of Health ricerca corrente (RRC).

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ensci.2024.100539>.

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