THE RELATIONSHIP BETWEEN CHRONIC KIDNEY DISEASE AND DEMENTIA AND PSYCHOLOGICAL IMPAIRMENT IN GERIATRIC PATIENTS: A SYSTEMATIC REVIEW

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Abstract

Background: Dementia is a growing concern, particularly among older adults with chronic kidney disease (CKD). Recent studies suggest a link between CKD and an increased risk of dementia.

Objectives: This systematic review aims to comprehensively assess the current research on the relationship between CKD and dementia in geriatric patients.

Methods: We conducted a systematic search of electronic databases like PubMed, MEDLINE, Science Direct, and Scopus. Two independent reviewers screened and extracted data from eligible studies.

Results: Eight studies including 239,844 participants in total and 95,760 (39.9%) males—were included in our data. The follow-up duration ranged from 6 months to 48 months. While a limited long-term link was suggested between CKD status and dementia and delirium, there is a co-occurrence of the detection of CKD and dementia in real-world clinical practice among the geriatric population. In patients with moderately severe CKD, lower scores on the mini-mental state examination (MMSE) and older age were risk factors for the advancement of cognitive dysfunction.

Conclusion: There is a heavy burden of dementia consecutive to CKD in the geriatric population. Better screening and treatment methods could be developed as a result of an improved understanding of causal factors, which could be facilitated by longitudinal research, brain imaging, and improved screening instruments.

Keywords: Chronic Kidney Disease (CKD)**,** Dementia**,** Geriatric Patients**,** Systematic review.

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Introduction

Globally, dementia and CKD are two prevalent illnesses that disproportionately impact elderly persons. Although every ailment poses distinct difficulties and complexities, an increasing body of research indicates a noteworthy correlation between the two. In order to provide senior patients with complete care who are managing both dementia and CKD, it is imperative to comprehend this interaction [1].

A reduction in cognitive function that causes problems in day-to-day functioning is referred to as dementia. Although there are many different kinds of dementia, Alzheimer's disease is the most prevalent kind. Dementia symptoms include personality changes, linguistic difficulties, and memory loss. Since dementia is a degenerative illness, a person's capacity to live independently may be greatly impacted as symptoms deteriorate over time [2].

The intricate interactions between CKD and dementia, as well as how they affect general health, are the link between the two illnesses. Research has indicated that patients with CKD are more likely than those with adequate renal function to have cognitive decline and dementia. Numerous variables are assumed to be at play here, including the kidneys' job in controlling blood pressure and preserving electrolyte balance, both of which can impact brain function [3].

Moreover, cerebrovascular illness, a prominent cause of dementia in older persons, can be made more likely by the presence of CKD. Cognitive deterioration can also be attributed to oxidative stress and chronic inflammation, both of which are common in CKD. Furthermore, drugs used to treat CKD, such as blood pressure and diuretics, may have adverse effects that affect cognitive performance [4].

On the other hand, the management of CKD can also be significantly affected by dementia. Delusions can make it difficult for a person to control their hydration intake, maintain dietary restrictions, or follow complex prescription regimens. Raising the risk of problems and degrading renal function can result from this. Delays in diagnosis and treatment can also result from people's inability to effectively convey their symptoms when they are cognitively impaired [5].

Given the connection between dementia and CKD, healthcare professionals must treat elderly individuals who are treating both disorders holistically. This entails routinely testing patients with CKD for cognitive impairment and keeping an eye on renal function in patients with dementia. Nephrologists, neurologists, and geriatric experts can collaborate to create customised treatment plans that are tailored to the individual requirements of each patient as part of interdisciplinary care teams [6].

Dementia is a growing public health concern, especially among geriatric populations. CKD is also prevalent in older adults. Recent studies suggest a link between CKD and an increased risk of dementia. This systematic review comprehensively analyses existing research to understand the relationship between CKD and dementia in older adults. This knowledge can inform strategies for preventing dementia in at-risk populations and improving care for geriatric patients with both conditions. The growing prevalence of dementia and CKD in geriatric populations necessitates a deeper understanding of the potential association between these conditions. This systematic review aims to synthesize current research evidence on the relationship between CKD and dementia in geriatric patients.

Study Objectives

- To systematically identify and assess relevant studies investigating the association between CKD and dementia in older adults.
- To evaluate the strength and consistency of the evidence for this association.
- To explore potential mechanisms underlying the link between CKD and dementia.
- To identify any limitations or gaps in the existing research.

Methods

This systematic review adhered to the guidelines set forth in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [7]. We conducted a comprehensive electronic search across bibliographic databases including PubMed, Web of Science, SCOPUS, and Science Direct. Our search strategy targeted English-language studies that explore the association between CKD and dementia in geriatric populations. We utilized relevant keywords related to both CKD and dementia to ensure a thorough search. To maintain objectivity, two independent reviewers screened the search results, selected studies meeting the inclusion criteria, extracted data, and assessed the methodological quality of the included research using established evaluation tools.

Eligibility Criteria

Inclusion criteria:

- Studies that investigate the relationship between CKD and dementia in geriatric patients.

- Studies with participants aged 65 years and older.
- Studies published in English.
- Studies that provide data on the prevalence, incidence, risk factors, or outcomes of dementia in geriatric patients with CKD.
- Randomized controlled trials, observational studies, cohort studies, case-control studies, or cross-sectional studies.

Exclusion criteria

- Studies that do not focus on CKD or dementia in geriatric patients.
- Studies with participants younger than 65 years of age.
- Studies published in languages other than English.
- Case reports, editorials, commentaries, letters, reviews without original data, and conference abstracts.
- Studies that do not provide relevant data on the relationship between CKD and dementia in geriatric patients.

Data Extraction

To ensure accuracy and consistency in the screening process, titles and abstracts retrieved from the search were evaluated for relevance to the study question according to the pre-defined inclusion and exclusion criteria. Reference management software like Rayyan (QCRI) [8] was utilized to facilitate efficient screening and reduce bias. Studies deemed relevant by at least one reviewer were progressed to full-text evaluation by both reviewers. Any disagreements regarding inclusion were resolved through discussion and consensus. Key information from the included studies, including titles, authors, publication year, study location, participant demographics (age, gender distribution, CKD diagnosis criteria), and primary outcomes related to the association between CKD and dementia, were extracted using a standardized data extraction form. Additionally, an established tool for methodological quality assessment was employed to evaluate the risk of bias within the included studies.

Data Synthesis Strategy

In order to provide a qualitative evaluation of the research findings and components, summary tables were generated using data extracted from relevant studies. Once the data collection for the systematic review is complete, the optimal approach for utilizing the data from the included studies will be determined.

Risk of Bias Assessment

For evaluating the study's quality, the Joanna Briggs Institute (JBI) [9] critical assessment criteria for studies reporting prevalence data was employed. This tool comprises nine questions, with positive responses assigned a score of 1 and negative, unclear, or irrelevant responses receiving a score of 0. Scores below 4, between 5 and 7, and above 8 will be classified as low, moderate, and high quality, respectively. Researchers independently assessed the quality of the studies, and any disagreements were resolved through discussion.

Results

Search results

After 402 duplicates were removed, a total of 812 study papers were found through a systematic search. After 410 studies had their titles and abstracts evaluated, 299 papers were discarded. Four articles were not located out of the 64 reports that were required to be retrieved. 107 papers were screened for full-text assessment; 62 were rejected because the study results were wrong, 33 because the population type was inaccurate, 2 articles were editor's letters, and 2 were abstracts. Eight research publications in this systematic review satisfied the requirements for eligibility. An overview of the procedure used to choose the research is illustrated in (Figure 1).

Sociodemographic features of the comprised studies

The research publications' sociodemographic information is displayed in (Table 1)**.** Eight studies including 239,844 participants in total and 95,760 (39.9%) males—were included in our data. Four studies were retrospective cohorts [10-13], two were prospective cohorts [15, 16], one was a case-control [14], and one was a cross-sectional study [17]. Three studies were conducted in the UK [10, 12, 13], two in the USA [16, 17], one in Australia [11], one in Egypt [14], and one in Taiwan [15]. The earliest study was conducted in 2005 [16] and the latest in 2023 [11].

Clinical outcomes

The clinical features are displayed in (Table 2). The follow-up duration ranged from 6 months [10] to 48 months [16]. While a limited long-term link was suggested between CKD status and dementia and delirium, there is a co-occurrence of the detection of CKD and dementia in real-world clinical practice among the geriatric population [10-14, 17]. In patients with moderately severe CKD, lower scores on the MMSE [15] and older age were risk factors for the advancement of cognitive dysfunction [15, 16].

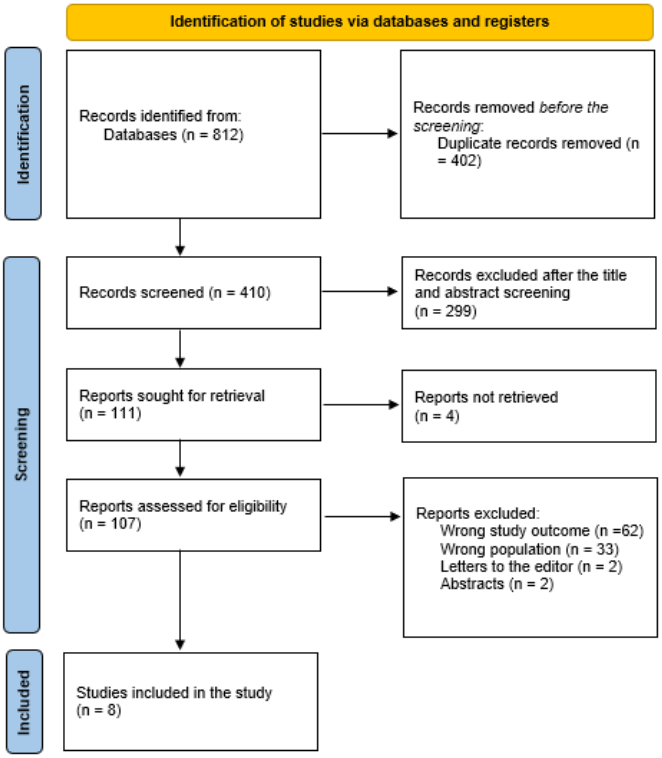

Figure 1. Study decision is summed up in a PRISMA diagram.

Discussion

This is the first systematic review to discuss the association between the incidence of dementia and CKD in the elderly population. We found that while a limited long-term link was suggested between CKD status and dementia and delirium, there is a co-occurrence of the detection of CKD and dementia in real-world clinical practice among the geriatric population [10-14, 17]. **Berger *et al.*** reported that early in CKD, cognitive changes take place, and skills deteriorate at varying rates. Particularly impacted are language orientation and attention. Patients' ability to participate in healthcare decision-making is probably going to be reduced by the cognitive effects of CKD [18]. In an integrative review by **Hannan *et al.*** also found that there are numerous, uneven methods used in the evaluation of cognitive function in older persons with CKD. It is essential in research and therapy to adequately measure cognitive performance in older adult patients with CKD by evaluating many cognitive domains, as there is currently no validated test of cognitive function for use in this population [19].

Vascular pathology is linked to CKD; nevertheless, the exact source of cognitive impairment in CKD is yet unknown. In general, people with CKD have higher rates of cerebrovascular illness and the classic risk factors for the condition, such as diabetes, stroke, myocardial infarction, and hypertension [20], all of which are linked to dementia and cognitive impairment. Additionally, as no memory domains account for the majority of cognitive impairment in CKD, researchers have conjectured about possible vascular etiologist. Theories on underlying shared processes that may mediate the kidney-cognition association are at the center of a lot of conjecture regarding the relationship between CKD and cognitive impairment. It is believed that non-traditional vascular risk factors that are associated with CKD, such as anemia, oxidative stress, increased inflammatory cytokines, and alterations in homocystine and lipid levels, can impact cognitive performance [21, 22].

We also found that in patients with moderately severe CKD, lower scores on the MMSE [15] and older age were risk factors for the advancement of cognitive dysfunction [15, 16]. The majority of these risk factors for cognitive impairment are common to both hemodialysis and CKD populations. However, compared to the general population, stroke and the high incidence of cardiovascular risk factors [23, 24] overwhelm the effects of aging and non-vascular variables.

Clinical implications and future directions

Table 1. The sociodemographic attributes of the participating populations.

Study	Study design	Country	Participants	Mean age	Males (%)
Hiramatsu et al., 2020 [10]	Retrospective cohort	UK	235004	75.1±9.7	93 233 (39.7%)
Igwe et al., 2023 [11]	Retrospective cohort	Australia	908	77.1 ± 7.2	534 (58.8%)
Sasaki et al., 2011 [12]	Retrospective cohort	UK	360	80.5 ± 7.6	191 (53%)
Hobson et al., 2022 [13]	Retrospective cohort	UK	92	75.9 ± 9.3	49 (53.3%)
Elgazzar et al., 2023 [14]	Case-control	EGYPT	100	68 ± 6.1	61 (61%)
Weng et al., 2012 [15]	Prospective cohort	Taiwan	125	78.6 ± 3.6	63 (50.4%)
Kurella et al., 2005 [16]	Prospective cohort	USA	3,044	73.5 ± 2.9	1461 (48%)
Rodríguez-Angarita et al., 2016 [17]	Cross-sectional	USA	251	76.4 ± 7.9	168 (66.9%)

Table 2. Clinical features and results of the included research.

Study	Follow-up (months)	Dementia prevalence (%)	Dementia diagnosis	Main outcomes	JBI
Hiramatsu et al., 2020 [10]	6	NM	Clinical-based	While a limited long-term link was suggested between CKD status and dementia, they did find a co-occurrence of the detection of CKD and dementia in real-world clinical practice, as well as a substantial competing risk of mortality in the association between CKD stage and dementia.	Moderate
Igwe et al., 2023 [11]	NM	15 (1.7%)	Clinical-based	Malnutrition and delirium are significantly correlated in this group of CKD patients (65 years of age and older) who are admitted to the ICU.	Moderate
Sasaki et al., 2011 [12]	NM	32 (9%)	Clinical-based	Incidence of dementia was highly correlated with CKD, regardless of age, sex, education level, or other vascular risk factors.	Moderate
Hobson et al., 2022 [13]	NM	6 (6.5%)	ACE III	It has been shown that the risk of dementia is much higher in people with CKD than in those without the condition. Additional comorbidities may compound the effects of CKD and raise the risk of dementia.	High
Elgazzar et al., 2023 [14]	36	39 (39%)	CERAD-NB	In comparison to controls, CKD cases have an odds ratio of 3.1 for having impaired clinical dementia rating scores.	Moderate
Weng et al., 2012 [15]	36	29 (23.2%)	CDR	In patients with moderately severe CKD, lower scores on the MMSE and older age were risk factors for the advancement of cognitive dysfunction.	Moderate
Kurella et al., 2005 [16]	48	NM	3MS	Elderly people with CKD have a higher chance of cognitive impairment, which is not entirely explained by other known risk factors.	High
Rodríguez-Angarita et al., 2016 [17]	NM	NM	Petersen's criteria	Patients with CKD frequently experience depression and cognitive impairment, with the former affecting almost half of the patients.	Moderate

*NA=Not-applicable

ACE III =Addenbrooke's Cognitive Examination III, CERAD-NB =Consortium to establish a registry for Alzheimer's disease neuropsychological battery, CDR= Clinical dementia rating scale, and 3MS= The Modified Mini-Mental

In order to evaluate several cognitive domains, including those that are most frequently impacted in patients with CKD, clinical evaluations that seek to evaluate cognitive function in patients with CKD should employ more than one test. In both practice and research, it is probably insufficient to evaluate a patient with CKD in just one cognitive domain. Given the evidence supporting the notion that measuring executive function is a critical and sensitive sign of cognitive impairment in CKD patients, it makes sense to include executive function assessment among the domains evaluated in all older adult patients with CKD who exhibit suspected cognitive impairment [25].

It is crucial for clinical practice that cognitive tests be used to assess older adult patients with CKD while taking into account the patient's other impairments and comorbidities. Tests like the digit sign substitution test necessitate motor speed, motor coordination, and visual acuity, as previously mentioned [26]. To prevent missing cases and accurately assess the extent of the cognitive impairment issue in older adult CKD patients, it is imperative to select appropriate cognitive tests that take into account the patient's other comorbidities and sensory deficiencies.

Limitations

The present review is subject to many limitations. Firstly, the evaluation of cognitive performance in patients with CKD was limited to studies where the mean participant age was over 65 years old. This excluded research that examined cognitive function in individuals with CKD who were not older people. It's possible that by using this criterion, pertinent research on cognitive impairment in CKD patients was excluded. It's probable that alternative measures of cognitive function would have been used if trials with patients whose mean age was under 65 had been included. However, due to the higher frequency of cognitive impairment in this demographic, the study's focus was on older persons with a mean age greater than 65. Future research should look into midlife and younger persons' cognitive function assessments. Despite these drawbacks, a comprehensive evaluation that exposed the range of assessment tools being used to measure cognitive function in older adult CKD patients was carried out.

Conclusion

There is a heavy burden of dementia consecutive to CKD in the geriatric population. Better screening and treatment methods could be developed as a result of improved understanding of casual factors, which could be facilitated by longitudinal research, brain imaging, and improved screening instruments.

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