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Association between migraine and risk of dementia: a systematic review and meta-analysis

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Abstract: Migraines, a prevalent neurological disorder, are increasingly linked to an elevated risk of dementia, including Alzheimer's disease (AD) and vascular dementia (VaD). This systematic review and meta-analysis examined 12 cohort studies with 465,358 participants to assess this association. The results showed a significant relationship between migraines and dementia risk (OR = 1.35, 95% CI: 1.21–1.50), particularly chronic migraines (OR = 1.48, 95% CI: 1.44–1.52). Women, younger individuals, and those with a family history of dementia were at higher risk. Shared vascular risk factors, neurovascular dysfunction, and hormonal influences are potential mechanisms underlying this link. Chronic migraine may act as an early marker for cognitive decline, highlighting the need for targeted interventions and vascular risk management in at-risk individuals. Further research is essential to explore causal pathways and prevention strategies to reduce dementia risk in migraine patients.

Keywords: Chronic migraines, neurological disorder.

Introduction: Headache disorders, including migraines, are among the most prevalent neurological conditions globally, affecting a significant portion of the population. Headache and dementia are both prevalent neurological conditions that significantly contribute to

daily dysfunction and reduced quality of life [1]. Headache disorders are even more widespread, affecting up to 46% of the adult population, making it the fifth leading cause of disability worldwide. While headache prevalence decreases significantly in adults over the age of 50, it remains a common complaint among the elderly. Tension-type headache (TTH), the most frequent type of primary headache, is typically characterized by bilateral, non-throbbing mild to moderate pain. With a lifetime prevalence as high as 78%, it represents a significant health burden despite its relatively lower intensity compared to migraines. Migraines, on the other hand, are more complex, presenting as recurrent attacks of moderate to severe, pulsating, unilateral head pain, often accompanied by nausea, photophobia, and phonophobia. The prevalence of migraines is approximately 16% in individuals aged 45–64 years, with a noticeable decline as people age. Migraines are chronic, debilitating conditions typically characterized by episodic or chronic headaches, which can severely impact an individual's quality of life [2-4]. Traditionally, migraines have been associated with various vascular risk factors, such as hypertension, stroke, and cardiovascular diseases [5]. However, emerging evidence suggests that migraines may also play a significant role in the development of cognitive decline and neurodegenerative diseases, including Alzheimer's disease (AD) and vascular dementia (VaD) [6-8].

Recent studies have shown that migraines, particularly chronic and severe forms, are associated with a range of neurological abnormalities that may contribute to cognitive impairment [9]. These include reduced cerebral blood flow, alterations in white matter integrity, and increased levels of neuroinflammation [10]. These findings highlight the complex interplay between migraine pathophysiology and long-term brain health, raising important questions about the potential role of migraines as a risk factor for dementia. Headache phase of migraines are has an indirect effect on cognitive abilities, although psychiatric conditions are not noted. It is also known that chronic migraine sufferers are more prone to severe cognitive challenges compared to those with infrequent episodes [11,12]. These challenges may include issues with attention, memory, and processing speed, along with task performance that require executive functions [13].

The meta-analysis revealed that individuals with migraines have reduced general cognitive and language function compared to those without migraines [14]. The prevalence of dementia is rising steadily worldwide, particularly as the global population ages. Dementia, the most common neurological disorder among the elderly, has been shown to have a prevalence of 6.0%, with 3.9% of cases being Alzheimer's disease (AD), 1.6% vascular dementia (VD), and 0.5% other forms of dementia. Due to its progressive nature, dementia is typically characterized by memory impairment, executive dysfunction, and behavioral disinhibition. The public health burden of dementia is expected to rise dramatically, with the number of patients projected to double every 20 years, reaching 65.7 million by 2030 as the population ages According to the Centers for Disease Control and Prevention (CDC), in 2014, it was estimated that five million adults aged 65 and older were living with dementia in the United States. This number is projected to nearly triple to almost 14 million by 2060, presenting a significant public health challenge as the population ages [15]. As dementia, especially AD and VaD, becomes more prevalent, understanding the potential risk factors associated with these conditions is becoming increasingly important [16]. In patients with migraines, structural brain changes such as reduced grey matter, white matter hyperintensities on MRI, and brain parenchymal defects have been observed, highlighting potential long-term impacts on brain health. These findings raise the possibility that migraine disorders, especially chronic or severe forms, may be associated with increased risks of cognitive decline and dementia in later life.

METHODS

The study aimed to investigate the association between migraine and dementia, including Alzheimer's disease (AD) and vascular dementia (VaD), in human subjects. Two reviewers independently conducted a manual search of PubMed, Cochrane Library, Embase, and Web of Science from 2001 to 2020, focusing on cohort, case-control, and longitudinal studies. A total of 12 cohort studies comprising 465,3528 participants were analyzed. Eligible studies reported risk measures such as hazard ratios (HRs), odds ratios (ORs), or relative risks (RRs) with corresponding 95% confidence intervals (CIs). Studies were excluded if they were not peer-reviewed, lacked relevant outcomes or necessary data, or involved participants diagnosed with dementia before the study's baseline to prevent reverse causality. Conference abstracts and studies with incomplete data were also excluded.

The inclusion criteria ensured that studies were focused on human subjects with migraine and dementia, reporting detailed and measurable outcomes. The quality of the included cohort studies was assessed using the Newcastle-Ottawa Scale (NOS), which evaluated selection, comparability, and exposure or outcome assessment. A random-effects model was used to estimate pooled ORs for the association between

migraine and dementia. Subgroup analyses were conducted based on sex, migraine type (episodic vs. chronic), and study design. Heterogeneity was assessed using the I^2 statistic, while publication bias was evaluated with funnel plots and Egger's test. The rigorous methodology and comprehensive analysis provided robust insights into the relationship between migraine and dementia risk.

RESULTS

Out of 45,872 records identified in the initial search, 32 studies met the eligibility criteria. The final analysis included 12 cohort studies, with a total of 465,358 participants. These studies involved patients with a variety of migraine types and included participants from different countries, with a mean follow-up of 10 years.

The pooled ORs indicated a statistically significant association between a history of migraine and an increased risk of dementia (OR = 1.35, 95% CI: 1.21–1.50), AD (OR = 1.49, 95% CI: 1.08–2.05), and VaD (OR = 1.72, 95% CI: 1.32–2.25). These associations remained significant even after adjustment for confounders such as age, sex, hypertension, and diabetes (Table 1).

Condition	Odds Ratio (OR)	95% Confidence Interval (CI)
Dementia	1.35	1.21–1.50
Alzheimer's Disease (AD)	1.49	1.08–2.05
Vascular Dementia (VaD)	1.72	1.32–2.25

Table 1. Combined ORs for Migraine and Risk of Dementia, AD, and VaD

Subgroup analysis revealed distinct patterns of dementia risk associated with migraines. Women with a history of migraine had a significantly higher risk of developing dementia compared to men (OR = 1.32, 95% CI: 1.16–1.51). Chronic migraine posed a greater risk for dementia than episodic migraine (OR = 1.48, 95% CI: 1.44–1.52). Additionally, participants under the age of 65 with a history of migraine demonstrated a significantly elevated risk of developing Alzheimer's disease compared to those without migraines (HR = 1.58, 95% CI: 1.52–1.64). These findings underscore the influence of sex, migraine type, and age on the association between migraine and dementia (Table 2).

Subgroup	Condition	Odds Ratio (OR)	95% Confidence Interval (CI)
Sex	Dementia (Women vs. Men)	1.32	1.16–1.51
Migraine Type	Chronic Migraine vs. Episodic Migraine	1.48	1.44–1.52
Age	Participants under 65 (Migraine vs. No Migraine)	1.58	1.52–1.64

Table 2. Subgroup Analysis of Dementia Risk Factors in Migraine Patients

In the cohort study using data from the National Health Insurance Service (NHIS), chronic migraine was found to be an independent risk factor for AD, with an HR of 1.72 (95% CI: 1.39–2.13). This study involved 10.6 million individuals and adjusted for age, sex, and comorbidities. Additionally, this cohort study demonstrated that individuals with a family history of dementia who also had migraine were at an even higher risk for developing AD and VaD.

DISCUSSION

Our findings provide robust evidence of an association between migraine and an increased risk of dementia, particularly Alzheimer's disease (AD) and vascular dementia (VaD). The pooled odds ratios (ORs) from the meta-analysis indicate a significant risk of developing dementia in individuals with a history of migraine (OR = 1.35, 95% CI: 1.21–1.50), AD (OR = 1.49, 95% CI: 1.08–2.05), and VaD (OR = 1.72, 95% CI: 1.32–2.25). These findings are consistent with earlier studies suggesting that migraine, especially chronic migraine, may be linked to neurovascular changes that predispose individuals to cognitive decline [17]. The observed association aligns with findings from the National Health Insurance Service (NHIS) cohort study, which found that chronic migraine was an independent risk factor for AD (HR = 1.72, 95% CI: 1.39–2.13) [18-20].

Several potential mechanisms could explain the

relationship between migraine and dementia. One of the most prominent factors is the shared vascular risk factors between migraine and dementia, such as hypertension, diabetes, and obesity [21-24]. These comorbidities are known to damage the vasculature, which may accelerate the development of both cognitive decline and migraine [25,26]. For example, hypertension and diabetes increase the risk of stroke, which in turn contributes to the development of VaD. Additionally, migraine attacks are thought to be associated with alterations in blood-brain barrier integrity and neuroinflammatory processes, which are also implicated in dementia pathogenesis [27-30].

Moreover, neurovascular dysfunction, which has been observed in individuals with chronic migraines, could further explain the increased risk of dementia. Cortical and subcortical changes, including grey matter atrophy, are common in chronic migraineurs and could predispose individuals to neurodegenerative diseases like AD [31-33]. Migraines may also act as a precursor to vascular changes that disrupt cognitive function in the long term [34-38].

Our analysis found that the risk of dementia is significantly higher in women with a history of migraine (OR = 1.32, 95% CI: 1.16–1.51) [39,40]. This finding is consistent with previous literature, which suggests that gender plays a significant role in the severity of dementia risk. Female migraineurs, especially those with chronic migraine, may be at a heightened risk due to hormonal influences, as estrogen is thought to impact both vascular health and neurodegenerative processes.

In terms of migraine type, chronic migraine was associated with a significantly higher risk of dementia compared to episodic migraine (OR = 1.48, 95% CI: 1.44–1.52). This supports the hypothesis that the more frequent and prolonged nature of chronic migraine increases the likelihood of neurovascular damage and cognitive decline [41].

The compounded risk of dementia in individuals with both migraine and vascular comorbidities, such as hypertension and diabetes, is a noteworthy finding. Studies have suggested that these comorbid conditions may exacerbate the risk of dementia in migraine sufferers by contributing to vascular dysfunction, which is a known pathway to cognitive decline. The presence of both conditions may act synergistically, leading to a greater overall burden on cognitive function [42,43].

A cohort study using data from the National Health Insurance Service (NHIS) demonstrated that chronic migraine was an independent risk factor for AD, with an HR of 1.72 (95% CI: 1.39–2.13). Furthermore, this study indicated that individuals with a family history of dementia who also had migraine were at an even higher risk for developing AD and VaD. These findings underscore the importance of identifying individuals with migraine who also have vascular risk factors, as they may be at a significantly elevated risk of dementia [44-48].

Hypertension, diabetes, and obesity are significant modifiable factors contributing to dementia risk in migraineurs, emphasizing the importance of managing these conditions to reduce long-term neurological complications [49]. Additionally, a family history of dementia presents a non-modifiable risk factor, further underscoring the potential genetic predisposition in these cases. Addressing modifiable risk factors through early intervention and preventive measures may play a crucial role in mitigating the heightened risk of dementia in this population [50-54].

While the evidence strongly suggests an association between migraine and dementia, it is essential to note that the relationship does not imply causality. Further research is needed to elucidate the underlying mechanisms and to determine whether treating migraine could reduce the risk of developing dementia. Longitudinal studies with larger sample sizes and more comprehensive data on vascular and genetic risk factors will be crucial in understanding how migraine contributes to dementia development [55,56].

Additionally, future research should focus on exploring potential interventions that could mitigate the risk of dementia in individuals with chronic migraine. These could include optimizing the management of vascular risk factors (e.g., hypertension, diabetes), enhancing migraine treatment strategies, and investigating whether medications targeting neuroinflammation or cerebrovascular health could offer protective benefits for those at higher risk of dementia

CONCLUSIONS

This review highlights a significant association between migraines and increased dementia risk, particularly with chronic migraines. However, the underlying pathophysiological mechanisms remain unclear. Further studies focusing on neurovascular changes, inflammation, and advanced diagnostic methods are needed to better understand and mitigate this risk.

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