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Does Diabetes have the potential to elevate the risk of Dementia? A Meta-Analysis

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Abstract

Background: The relationship between diabetes and the risk of developing dementia remains inadequately understood. This study assesses the factors associated with the onset of dementia in individuals with diabetes, offering insights for the prevention of dementia among diabetic patients.
Aim: To find out the factors associated with onset of Dementia in Diabetic individuals.
Materials & Methods: This analysis employed databases including PubMed, Embase, Web of Science, and the Cochrane Library to examine literature from January 1, 2012, to March 31, 2024. Articles underwent a thorough evaluation based on defined inclusion and exclusion criteria. The Newcastle-Ottawa Scale (NOS) was employed to assess the quality of the studies.
Results: The research examined 14 articles, and the meta-analysis indicates a significant correlation between diabetes and a heightened risk of dementia. A diabetes duration of under five years is associated with an increased risk of dementia.
Conclusion: Diabetes significantly elevates the risk of dementia, especially in cases where the duration of diabetes is less than five years or when hypoglycaemia occurs.

1.INTRODUCTION

Diabetics have high blood sugar due to hyperinsulinism or insulin resistance[1]. Global diabetes cases rose from 463 million in 2019 to over 537 million in 2021, according to the IDF. In developing nations like India and China, prevalence is expected to grow 46% by 2045 [2,3]. High blood sugar can damage nerves, blood vessels, the heart, kidneys, and retina, reducing life quality and creating serious health hazards [4]. Tests show that elevated blood sugar causes reactive oxygen species, which cause neuroinflammation and neuronal loss in the hippocampus, decreasing cognitive function and perhaps causing dementia[5,8] . Diabetes increases cognitive impairment and dementia risk, according to systematic reviews [9].

A severe neurological disease, dementia, greatly impairs daily life. Over 550,000 people worldwide are diagnosed with dementia each year, with almost 100,000 new cases; more than 60% of these instances occur in low- and middle-income countries[10] . Age is a major risk factor for dementia, and diabetes worsens neuron and blood vessel damage. Kapil Gudala et al.'s 2013 meta-analysis found that diabetics have a 73% greater risk of dementia, including a 56% higher risk of Alzheimer's Disease (AD)[11]. Further studies show that diabetes doubles the risk of all-cause dementia, including vascular dementia and AD[12]. Previous studies have indicated that diabetics had a twice-higher risk of all dementias, including AD and vascular dementia [13]. Reviews show that diabetes, hypertension, dyslipidemia, and obesity predict dementia in people over 65 [14].

A comprehensive systematic review and meta-analysis examined whether diabetes and dementia risk have changed. Based on Kapil Gudala et al.'s 2013 meta-analysis, this study covers 2012-2024. Its objective is to quantify the correlation between diabetes and dementia, assess factors that may influence this relationship, and compare current findings with 2013 results to discover any changes in risk over the last decade.

2.MATERIALS AND METHODS

A comprehensive literature search was performed utilizing PubMed, Embase, Web of Science, and the Cochrane Library, covering the period from January 1, 2012, to March 31, 2024. The investigation concentrated on the integration of "Diabetes Mellitus" with "Dementia."

Inclusion criteria: Research involving adult subjects. Research investigating the correlation between diabetes and the risk of developing dementia. Studies utilizing cohort, cross-sectional, and various observational methodologies

Exclusion criteria: Papers that focus solely on dementia or diabetes without examining the risk relationship between the two conditions. Animal studies or cellular research. Reviews, conference articles, guidelines, and other forms of non-original research. Non-English publications. Studies involving fewer than 30 participants exhibit limited generalizability.

Collection of data:

Authors independently assessed titles and abstracts to identify unsuitable articles before extracting data. The full texts of possibly relevant research were then carefully evaluated for inclusion.

Authors independently collected and verified data in a consistent format. Author, publication years, study designs, locations, sample sizes, participant demographics (age, gender, race), follow-up durations, and diabetes and dementia diagnostic criteria were extracted.

3.ASSESSMENT OF QUALITY

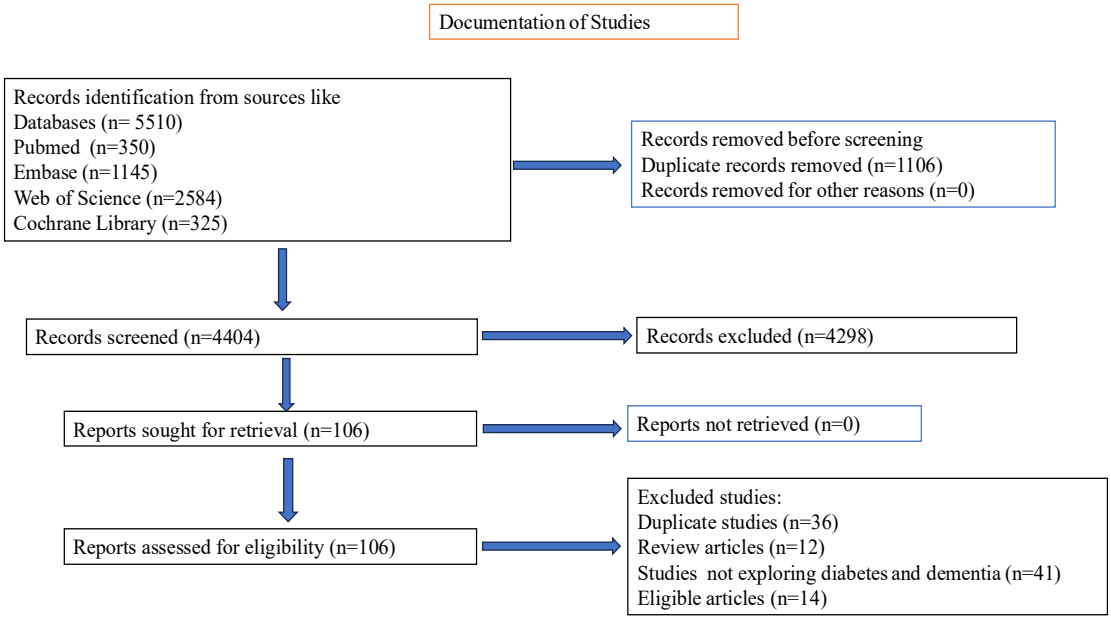
The Newcastle-Ottawa Scale (NOS) was employed to assess the quality of the studies included in the analysis. This instrument evaluates three dimensions based on eight criteria, allowing for comparability scoring of up to 2 points, while the remaining criteria are scored at 1 point each. Research studies that received scores between 7 and 9 were classified as high quality, whereas those with scores ranging from 4 to 6 were categorized as moderate quality. Two evaluators independently assessed each study and verified their evaluations against one another. Discrepancies were addressed via consultation with a researcher.

4.STATISTICAL ANALYSIS

Diabetes was the primary endpoint in this study to determine how diabetes affects dementia risk. Statistics were processed using Stata 15.0 and R 4.2.1. Heterogeneity was measured using Cochran's Q test and Higgins I^2, using a random-effects model for significant heterogeneity ($P < 0.10$ or $I^2 > 50\%$). Egger's and Begg's tests and funnel plots assessed publication bias. P-value < 0.05 was used to assess the statistical significance of the findings.

5.RESULTS

A systematic PubMed, Embase, Web of Science, and Cochrane Library search found 5,510 articles. Initial screening eliminated 4,404 articles with titles and abstracts that did not match the inclusion criteria after deleting 1106 duplicates. This process selected 106 articles for further analysis. After full-text examination, 92 papers were removed for being irrelevant to the study's emphasis on diabetes and dementia, review articles, or duplicate data. The analysis included 14 papers.



5.STUDY CHARACTERISTICS

This review comprised 14 publications [15-29], 11 cohorts, and 3 cross-sectional studies. These 2012–2024 studies examined diabetes and dementia risk. Only one study addressed Type 1 diabetes [17].Most focused-on Type 2. Six [16,18,21,22,25,28] studies did not specify the kinds. These studies included 11,121,868 people, 9,543,502 of whom had diabetes. Of these, 30,500 dementia cases were reported; however, not all studies provided statistical data [18-24]

Table 1 lists demographics and diagnostic criteria.

Details of the study population	Male: Female	Mean Age	Type of diabetes	Diagnostic criteria for dementia	Regression method	Follow-up duration (QR)
A study in Canada included approximately 3 lakh diabetic individuals [15]	1:1 ratio	45.6	Type 2 diabetes	ICD-10	Cox	5 years (8)
Another study by Kim in Korea studied 8,500,000 patients [16]	1.5:1	61.4	Type 2	ICD 10	Cox	6 years (7)
A study conducted in Australia included 11,000 subjects [17]	1.3:1	65.8	Type 2	DSM-IV	Logistic	5 years (7)
In Britain, Amidei included 10,000 diseased patients [18]	1.2:1	76.8	Type 2	ICD-10	Cox	1 year (9)
In Sweden, Javanshir identified 268 diabetes study subjects [19]	1:1	82.3	Not classified	The National Institute on Aging	Cox	Not followed up (10)
Secnik in Sweden studied 1200 samples[20]	1:3	73.2	Type 2	ICD-10	Logistic	Not followed (11)
Salinas in Mexico studied 11,000 subjects[21]	1:3	73.2	Type 2	DRG	Poison	3 years (7)
Frison in France identified 8000 individuals [22]	1:2	73.5	Not classified	DSM-IV	Cox	8 years (8)
In China, Ma studied 8000 samples[23]	1:1	75.81	Not classified	DSM-IIIR	Cox	4 years (8)
In 2016, Chin identified 2000 Korean subjects [24]	1:1	67.5	Type 2 diabetes	KCD-6	Cox	3 years (8)

Gennip in the Netherlands studied 90,000 subjects [25]	1:1	57.1	Type 2 diabetes	ICD-9	Cox	9 years (9)
Jia in China studied 4500 subjects [26]	1:1	71.32	Not classified	DSM-IV	Cox	Not reported (12)
Kuo in China identified 35,000 individuals [27]	1.5:1	48.74	Type 1 diabetes	ICD-9	Cox	Incomplete follow-up time (6)
Lee in Korea studied 8 lakh individuals [28]	1:1	41.2	Not classified	ICD-10	Cox	7 years (8)

The relation between diabetes and dementia

Eight of 14 studies examined hyperglycaemia and dementia onset. A random-effects model was used due to significant heterogeneity in these investigations. Table 2 showed that diabetics had a considerably higher dementia risk. An RR of 1.59 for All Types of Dementia (ATD) among diabetics was consistent with a 2013 meta-analysis.

Table 2: Risk of dementia in diabetes subjects.

No. of studies involved	RR (CI)	P value
9 studies	1.59 (1.40-1.80)	0.0001

6.DISCUSSION

This meta-analysis of 14 observational studies found that diabetics have a 59% higher risk of dementia than non-diabetics. This matches a 2013 meta-analysis.

Diabetes and dementia have been studied. In their meta-analysis of 1,455 adult diabetes patients tracked for 14 years, 101 got dementia and 77 had AD, a 66% increase[29]. Salinas et al. found that Mexican type 2 diabetics had twice the dementia risk of non-diabetic [21].. A major prospective cohort study in Rotterdam, the Netherlands, found that diabetes nearly doubles dementia and AD risk [30]. A systematic evaluation of 243 prospective studies and 153 randomized control trials found that diabetes increased AD risk by 69% [31]. Another study found that diabetics have a 1.25 to 1.91 times higher risk of cognitive impairment and dementia, even in early stages [32].

These studies demonstrate a strong link between diabetes and dementia, which may start in the first five years. The mechanisms of this association are still unknown.

Diabetes problems include insulin resistance, acute blood glucose swings, blood flow rate abnormalities, and chronic inflammation may raise dementia risk, according to biological studies. Diabetes-induced neuronal death and dementia are linked to decreased hippocampus CA1 and CA3 granule cell proliferation. Brain damage from diabetes includes cerebral atrophy, altered brain vasculature, decreased synaptic plasticity, and neuroglial cell dysfunction [33-35].Imaging and neuropathological investigations suggest that diabetic brains may change like early-stage AD brains[12,36]. AD is characterized by amyloid-beta (Aß) protein buildup, Tau protein hyperphosphorylation, and neurofibrillary tangle development, leading to dementia[37].

Recent studies show that Type 2 diabetes (T2D) causes dementia and cognitive deficits[38]. Due to T2D prevalence and patient self-management issues, dementia is projected to rise[39]. Diabetes duration may affect dementia onset, but more research is needed. The American ARIC study found that dementia risk increases with diabetes duration[40]. Studies show that cognitive performance diminishes dramatically in the first few years following diabetes onset, regardless of age[41,42]. According to our findings, diabetes increases the risk of dementia by 29% in less than five years, suggesting that the condition may start early. A UK prospective study found a 15% increase in dementia incidence for every five years of diabetes duration, blood sugar control, and diabetes duration[43]. Similar to our findings, a German prospective study reported greater dementia rates in the early stages of diabetes, suggesting that persistent aberrant blood sugar levels may cause cognitive impairment before diabetes is clinically recognized[44].Our research shows that hypoglycaemia incidents considerably increase diabetes dementia. Hypoglycaemia, a common acute diabetic consequence, can damage brain arteries, causing neuronal destruction and cognitive impairment[20,45,46]. Diabetics with severe hypoglycaemia are more likely to acquire dementia, according to cohort studies. Severe hypoglycaemia episodes are linearly related to dementia risk, especially in AD patients. Even one severe episode increases mortality risk, regardless of dementia 47.

Further studies show that older T2D patients with severe hypoglycaemia have a greater dementia risk, suggesting a bidirectional link [48,49]. Our findings show that diabetics with hypoglycaemic episodes had a 56% higher risk of dementia than those without, demonstrating the negative effects of hypoglycaemia on brain function and dementia.

A systematic study found that severe hypoglycaemia incidents increase dementia risk [RR: 1.47, 95%CI (1.24–1.74)]. One episode increases risk by 29% [RR: 1.29, 95%CI (1.15–1.44)], two episodes by 68% [RR: 1.68, 95%CI (1.38–2.04)], and three or more episodes double the risk [RR: 1.99, 95%CI (1.48–2.68)][50]. These data show that hypoglycaemia incidents significantly contribute to dementia in diabetics.

7. CONCLUSION

The findings of our research indicate that individuals with diabetes face a heightened risk of developing dementia, aligning with the conclusions of a study carried out in 2013. Future research should employ larger sample sizes and adopt a longitudinal approach to more effectively examine various risk factors. Future research should include a broader spectrum of dementia types and diabetes, expand the range of studies analysed, increase the volume of data, and assess the impact of measurement errors on risk estimates.

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