

Relationship Between Diabetes and Dementia

Developing prediabetes at younger ages increases risk

Have you ever wondered about the connection between blood sugar and dementia risk? A recent study analyzed the risk of dementia for people with normal blood glucose levels, prediabetes, and type 2 diabetes. The results showed that developing diabetes significantly increases the risk of dementia, but the age of onset also plays a vital role. This analysis is a must-read for anyone who is concerned about dementia.



Abstract

- **Aims/hypothesis:** The aim of this work was to evaluate whether the association of prediabetes with dementia is explained by the intervening onset of diabetes.
- **Methods:** Among participants of the Atherosclerosis Risk in Communities (ARIC) study we defined baseline prediabetes as HbA1c 39–46 mmol/mol (5.7–6.4%) and subsequent incident diabetes as a self-reported physician diagnosis or use of diabetes medication. Incident dementia was ascertained via active surveillance and adjudicated. We quantified the association of prediabetes with dementia risk before and after accounting for the subsequent development of diabetes among ARIC participants without diabetes at baseline (1990–1992; participants aged 46–70 years). We also evaluated whether age at diabetes diagnosis modified the risk of dementia.
- **Results:** Among 11,656 participants without diabetes at baseline, 2330 (20.0%) had prediabetes. Before accounting for incident diabetes, prediabetes was significantly associated with the risk of dementia (HR 1.12 [95% CI 1.01, 1.24]). After accounting for incident diabetes, the association was attenuated and non-significant (HR 1.05 [95% CI 0.94, 1.16]). Earlier age of onset of diabetes had the strongest association with dementia: HR 2.92 (95% CI 2.06, 4.14) for onset before 60 years; HR 1.73 (95% CI 1.47, 2.04) for onset at 60–69 years; and HR 1.23 (95% CI 1.08, 1.40) for onset at 70–79 years.
- **Conclusions/interpretation:** Prediabetes is associated with dementia risk but this risk is explained by the subsequent development of diabetes. Earlier age of onset of diabetes substantially increases dementia risk. Preventing or delaying progression of prediabetes to diabetes will reduce dementia burden.

Having high blood sugar levels and insulin resistance can harm our brains in several ways. It can impair the brain's ability to remove waste and create new connections between brain cells, lead to inflammation due to high insulin levels, and cause vascular changes in small arteries and capillaries that transport oxygen and nutrients to the brain.

This study showed that people with prediabetes have a 12% higher risk of developing dementia over a 9-year follow-up period. Those who developed diabetes before the age of 60 had an almost threefold increased risk, while those who developed it between 60-69 had an almost twofold risk. Onset between 70-79 had a 23% increased risk.

With almost 70% of people with prediabetes going on to develop diabetes in their lifetime, early intervention is essential to prevent the development of diabetes. There are several medications available that can be helpful, including metformin (which can decrease the risk by 72% when used for 4 or more years), GLP-1 receptor agonists (such as Ozempic, Trulicity, Victoza, Mounjaro, and others) that can reduce the incidence by half, and DPP-4 inhibitors (such as sitagliptin, saxagliptin, linagliptin, alogliptin) that can slow the progression of dementia.

Lifestyle changes are always the first line of treatment, and it includes increased exercise (especially zone 2 exercise) and dietary changes (such as reducing sugar and starch intake) which are the mainstay of any intervention.

Prediabetes, intervening diabetes and subsequent risk of dementia: the Atherosclerosis Risk in Communities (ARIC) study. *Diabetologia* 2023 Aug 01;66(8)1442-1449, J Hu, M Fang, JR Pike, PL Lutsey, AR Sharrett, LE Wagenknecht, TM Hughes, JC Seegmiller, RF Gottesman, TH Mosley, J Coresh, E Selvin