Study shows dementia risk increases the earlier a person develops diabetes

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New research published in *Diabetologia* shows an association between type 2 diabetes (T2D) and developing dementia in later life—with the risk of dementia increasing the earlier a person develops T2D. The study

is by Ph.D. student Jiaqi Hu and Professor Elizabeth Selvin of the Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, U.S., and colleagues.

Their study investigated the association between prediabetes and dementia. Prediabetes is an intermediate stage of high blood sugar, where blood sugar is high but has not yet crossed the threshold for T2D. Prediabetes confers a high risk of progression to diabetes but is also independently associated with other clinical outcomes. Most people who develop T2D first pass through this "window" of prediabetes.

The risk of progression to T2D among people with prediabetes is substantial; among middle-aged adults with prediabetes, 5%–10% per year go on to develop T2D, with total of 70% of those with prediabetes progressing to T2D during their lifetime. In the U.S., up to 96 million adults have prediabetes, accounting for 38% of the adult population.

To understand the risks of dementia associated with prediabetes, the authors analyzed data from participants of the Atherosclerosis Risk in Communities (ARIC) study. Those enrolled were aged 45–64 years in 1987–1989 and from four U.S. counties: Forsyth County, North Carolina; Jackson, Mississippi; suburbs of Minneapolis, Minnesota; and Washington County, Maryland. The baseline period for the analysis was visit 2 of the study (1990–1992), which was the first time where HbA1c (glycated hemoglobin—a measure of blood sugar control) and cognitive function were measured in this study.

The cognitive function assessments incorporated data from a scoring system involving three cognitive tests, administered at visits 2 (1990–1992) and 4 (1996–1998), the expanded neuropsychological ten-test collection, administered from visit 5 (2011–2013) onwards and informant interview (Clinical Dementia Rating [CDR] scale and the Functional Activities Questionnaire [FAQ]). The Mini-Mental State

Examination (MMSE) was also administered. Participants were followed up until 2019.

The authors defined prediabetes as glycated hemoglobin (HbA_{1c}—a measure of blood sugar control) of 39–46 mmol/mol (5.7%–6.4%). They also looked at subsequent diagnoses of T2D during follow-up.

The authors evaluated the association of prediabetes with dementia risk before and after accounting for the subsequent development of T2D among ARIC participants with prediabetes at baseline. This was done to understand how much of the association of prediabetes with dementia was explained by progression to diabetes. They also evaluated whether age at diabetes diagnosis modified the risk of dementia.

Among 11,656 participants without diabetes at baseline, 2,330 (20%) had prediabetes. When accounting for diabetes that developed after the baseline period, they authors found no statistically significant association between prediabetes and dementia. However, they found that earlier age of progression to T2D had the strongest association with dementia: a three times increased risk of dementia for those developing T2D before age 60 years; falling to a 73% increased risk for those developing T2D aged 60–69 years and a 23% increased risk for those developing T2D aged 70–79 years. At ages 80 years or older, developing T2D was not associated with an increased risk of dementia.

The authors conclude, "Prediabetes is associated with dementia risk, but this risk is explained by the development of diabetes. Diabetes onset at early age is most strongly related to dementia. Thus, preventing or delaying the progression of prediabetes to diabetes will substantially reduce the future burden of dementia."

More information: Jiaqi Hu et al, Prediabetes, intervening diabetes and subsequent risk of dementia: the Atherosclerosis Risk in

Communities (ARIC) study, *Diabetologia* (2023). DOI: 10.1007/s00125-023-05930-7

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