**Hypoglycaemia is associated with dementia in individuals with type 2 diabetes mellitus: a systematic review, meta-analysis and meta-regression**

**ABSTRACT**

**Aim**

To quantify prospective associations of hypoglycaemia with all-cause dementia and its subtypes along with cognitive decline in people with type 2 diabetes mellitus (T2DM).

**Methods**

We systematically searched Embase and MEDLINE (January 2000–October 2024) for studies, in people with T2DM, reporting longitudinal associations of hypoglycaemia with any of the following outcomes: cognitive decline, all-cause dementia, Alzheimer’s disease (AD), or vascular dementia (VaD). Risk of bias was assessed using a modified Newcastle-Ottawa Assessment Scale for cohort studies. Data were meta-analysed using a random-effects model with empirical Bayes estimator for heterogeneity. A meta-regression was performed for the following covariates: age, sex, diabetes duration, smoking, follow-up length, comorbid hypertension, kidney disease, dyslipidaemia and stroke. Cumulative and leave-one-out meta-analyses were done as sensitivity analyses.

**Results**

Sixteen studies representing 3,758,910 individuals with diabetes were included. Meta-analysis showed hypoglycaemia was significantly associated with all-cause dementia (HR (95% CI) 1.49 (1.29, 1.72)) and AD (HR (95% CI) 1.31 (1.11, 1.54)). The single study examining hypoglycaemia and risk of VaD reported a significant association with a HR (95% CI) of 1.29 (1.11, 1.49). The pooled effect size did not significantly vary for any of the included covariates in meta-regression of all-cause dementia (all *P*>0.05). There was no effect of publication time and no undue influence of any individual study in cumulative and leave-one-out analyses. A positive association existed between hypoglycaemia frequency and all-cause dementia or its subtypes. For all-cause dementia, maximum HRs of 2.36–2.60 were observed in people with the highest frequency of hypoglycaemia. There is limited evidence to support a relationship between hypoglycaemia and cognitive decline.

**Conclusion**

Having a history of hypoglycaemia was related to higher risks of future all-cause dementia, AD and VaD in people with T2DM. The risk of dementia increased as the number of hypoglycaemic events increased.