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ASSOCIATION BETWEEN GLYCEMIC VARIABILITY AND LOWER COGNITIVE FUNCTION, MEDIATED BY ARTERIAL STIFFNESS, IN ASIANS WITH TYPE 2 DIABETES

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INTRODUCTION

Glycemic variability involves deleterious cellular processes due to hyperglycemic spikes and hypoglycemic troughs. It is a known predictor of renal, retinal, and cardiovascular complications in type 2 diabetes (T2D). However, its role in the development of cognitive impairment is unclear. Arterial stiffness damages cerebral microvessels with high pulsatile flow. We aimed to examine the association between glycemic variability and cognitive function, and the role of arterial stiffness in mediating the association.

METHODOLOGY

This was a cross-sectional study of participants from the Singapore Study of Macroangiopathy and Microvascular Reactivity in Type 2 Diabetes (SMART2D) cohort. Cognitive function was assessed with a Repeatable Battery for Assessment of Neuropsychological Status (RBANS). Pulse wave velocity, an index which reflects arterial stiffness, was measured using the applanation tonometry method. HbA1c readings were retrospectively extracted from medical records over a mean period of 3.2 years (up to 7.1 years). HbA1c variability was expressed as the HbA1c coefficient of variation (CV) calculated as standard deviation (SD) in intrapersonal HbA1c divided by intrapersonal mean HbA1c. Linear regression was used to examine the association between HbA1c CV and RBANS score, adjusting for demographics, APOE \$4\$ allele, and clinical covariates.

RESULTS

There were 1408 participants with a mean age of 61.4 ± 8.0 years. The mean number of HbA1c measurements was 9.9 ± 8.4 . Compared to HbA1c CV Quartile (Q) 1, HbA1c CV Q4 (highest HbA1c CV group) was associated with lower RBANS total score (indicative of lower cognitive function) with coefficients -1.52 (95% Confidence Interval (CI) -2.83 to -0.21; p = 0.023) and -1.49 (95% CI: -2.79 to -0.20, p = 0.024) in unadjusted and adjusted analyses respectively. Hb1A1c CV Q4 was also associated with a lower RBANS score in the attention domain with a coefficient of -2.19 (95% CI: -3.99 to -0.39, p = 0.017) in a fully adjusted analysis. In the mediation analysis, higher PWV accounted for 11.3% of the association between HbA1c CV Q4 and lower RBANS score in the attention domain.

CONCLUSION

Long-term glycemic variability was independently associated with lower cognitive function both globally and in the attention domain with mediation by arterial stiffness. HbA1c variability may be a potential biomarker to complement the use of HbA1c alone in T2D management.

KEYWORDS

type 2 diabetes, glycemic variability, cognitive function, arterial stiffness