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Correlation Between Uncontrolled Blood Glucose Levels And The Development And Progression Of Alzheimer's Disease in Type 2 Diabetes Mellitus Patients

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According to the U.S Department of Health and Human Services, Alzheimer's disease is ranked as the sixth leading cause of death in the United States. Experts suggest that more than five million Americans may have Alzheimer's. Alzheimer's is considered to be an irreversible and progressive neurodegenerative disease that gradually destroys memory, thinking skills, and ultimately becomes severe enough to interfere with activities of daily living. The majority of people with Alzheimer's disease are 65 and older, however, five percent of people have an early onset in their 40s or 50s. [1] Type 2 Diabetes Mellitus (Type 2 DM) also known as noninsulin-dependent diabetes, results from a combination of insulin resistance, inadequate insulin secretion, and excessive or inappropriate glucagon secretion. Numerous studies show a correlation between type 2 diabetes and Alzheimer's disease. Alzheimer's has been described as a form of diabetes that selectively involves the brain and has molecular and biochemical features that overlap with type 1 and 2 and the term type 3 diabetes has been proposed for Alzheimer's disease. [2]

We conducted a systematic literature review and included cohort studies systematic review articles, and retrospective studies. The search strategy included the following terms in different combinations: "Alzheimer's", "type 2 diabetes", "uncontrolled blood glucose", "cognitive impairment". 74 articles published within the past ten years were identified using Pubmed and Google scholar. Of these, 50 relevant articles from the past five years were utilized.

Research has consistently demonstrated that when hyperglycemia is present in the brain, insulin resistance becomes a major risk factor for Alzheimer's Disease development and progression. [2] Studies have shown that Alzheimer's and Type 2 Diabetes Mellitus have the same risk allele suggesting common pathogenic mechanism underlying the development of both Alzheimer's Disease and Type 2 DM. [3] The common observation for both Type 2 DM and Alzheimer's is desensitization of insulin receptors in the brain. Insulin acts as a growth factor in the brain and is neuroprotective, activates dendritic sprouting, regeneration and stem cell proliferation. The impairment of this important growth factor signal may facilitate the development of Alzheimer's Disease. [4] Functional enrichment analysis found lipid metabolism related pathways to be common between these two disorders. [5] Insulin resistance and deficiency can interact with amyloid-β protein and tau protein phosphorylation, each leading to the onset

and development of Alzheimer's Disease. [6] Type 2 DM increases the risk of dementia more than 2-fold. On the other hand, sulfonylureas may decrease the risk of dementia, as does metformin; together, these two Oral Hypoglycemic Agents decrease the risk of dementia in Type 2 DM patients by 35% over 8 years. [7] GLP-1 analogues show promise in providing novel treatments that may be protective or even regenerative in AD and Parkinson's Disease, something that no current drug does. [8] Intranasal insulin therapy may have beneficial effects on cognition and function in patients with AD.

In summary, pathophysiological and genetic similarities exist between Type 2 DM and Alzheimer's Disease, which include Insulin resistance and deficiency, Protein aggregation, Oxidative stress, Inflammation auto-phagocytosis, Advanced Glycation End Products (AGEs) and same risk allele. AD is often referred to as Type 3 diabetes. Insulin-resistance associated conditions are amenable to both pharmacologic and lifestyle interventions that may reduce the deleterious impact of insulin resistance on the aging brain. [9] Anti-diabetic drugs are currently used to successfully reduce the cognitive decline in Alzheimer's patients. Overall, our research adds to raising awareness among Type 2 DM patients to prevent the development, as well as the progression of Alzheimer's Disease.

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