

## A Review on Relationship between Type II Diabetes and Cognitive Impairment

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**Received:** 12 July 2018

**Accepted:** 25 August 2018

**Published in November 2018**

### Abstract

The association between diabetes and cognitive impairment is controversial. This systematic review examines the relationship of Cognitive Impairment in people with diabetes mellitus. The incidence of "Cognitive Impairment" was higher in individuals with diabetes than in those without diabetes in nine of ten studies reporting this aggregate outcome. These findings showed an associated between type II diabetes with an increased risk of cognitive impairment. However, the wide variations in the method between studies lead to a different interpretation of the conclusions.

**Keywords:** Cognitive impairment, Alzheimer's disease, Type 2 diabetes mellitus

### Introduction

Diabetes mellitus (DM), is a group of metabolic disorders in which there are high blood sugar levels over a long period of time (1). DM is correlated with vasculopathy and cerebrovascular diseases. The vasculopathy often proposed to play a role in the relationship between DM and cognition is cerebrovascular disease. Also, vasculopathy in combination with the neuropathological symptoms of alzheimer's disease, amyloid plaques and neurofibrillary tangles increase the risk for cognitive deficits. There is a link between cognitive deficit and DM. Compared to people without diabetes; DM patients have

1.2 to 1.5 fold greater rate of cognitive dysfunction.

Type 2 diabetes mellitus (T2DM) always is associated with increased risk of cognitive decline (2). Even prediabetes stages and insulin resistance status are associated with increased risk of cognitive decline and brain atrophy. In T2DM, cognitive changes mainly affect learning and memory, mental flexibility and psychological speed. Several studies of numerous demographic profiles have shown that cognitive decline is embittered in old people with type 2 diabetes. The decisive factors of this accelerated cognitive decline,

however, are less clear (3). The association between diabetes and changes in cognition is now well established, but the relation between diabetes and mild cognitive impairment (MCI) is an area of debate. In a previous systematic review, the writer found that diabetes was a risk factor for dementia (including Alzheimer's disease, vascular dementia and any dementia), but at that time, there were few detailed epidemiological data about the associations of diabetes with dementia risk factors, and high-quality studies should be started (4). In the systematic reviews, major studies showed diabetes was a risk factor for dementia, but not all (5). Typically, diabetic patients are not usually evaluated for cognitive function (6). Some Studies showed that insulin is needed for learning and memory. Insulin affects the metabolism of amyloid beta and neurofibrillary tangles in the brain which is the major pathological findings of cognitive deficits (7).

### **The association of diabetes with cognitive deficit**

Past reports published from longitudinal studies described the evaluation of cognitive function in people with diabetes. Comprehensive electronic searches for articles using Medline, EMBASE and Psyc INFO to identify studies that have been reported a large number of individuals who had T2DM.

In a study conducted by Lowe (8) to explore the relationship between T2DM and cognitive function in older Native Americans, cognitive function was assessed in 80 diabetic and 81 non diabetic Native Americans who were 45–76 years old. They found diabetes was associated with impairment on only two tests of cognitive function: verbal fluency ( $P=0.004$ ) and similarities ( $P=0.010$ ). In the same way a literature search of three databases was performed by Stewart and Liolitsa (9) to examine the evidence of association between cognitive impairment or dementia and the presence of T2DM. They found there is an association between T2DM and cognitive impairment. There is also evidence to increase

the risk of Alzheimer's disease in T2DM, and a strong interaction with other factors such as high blood pressure, dyslipidemia (9).

Another study which supports previous studies carried out by Edward and et al (10), to determine whether older women with diabetes have an increased risk of cognitive impairment. Three tests of cognitive function, the digit symbol test, the trails B test, and a modified version of the mini-mental state examination (m-MMSE), were administered by physician. Results showed women with diabetes ( $n=682$ ) had lower scores than those without diabetes on all 3 tests of cognitive function. Diabetes was also associated with increased odds of cognitive impairment (odds ratio = 1.63; 95% confidence interval, 1.20–2.23). Women who had diabetes for more than 15 years had a 57% to 114% greater risk of major cognitive impairment than women without diabetes (10).

Along with previous studies, Fontbonne and et al. (11) designed a study to compare 4 years changes in cognitive performance among elderly subjects. Subjects without any detectable cognitive dysfunction were classified into; normal, impaired fasting glucose, or diabetic. Their cognitive abilities were assessed by a global test (MMSE). Results showed after 4 years, diabetic subjects had a lower performance on all tests except the MMSE. In addition, diabetic patients tended to have an undesirable improvement in cognitive function for more than 4 years compared to those who had normal glucose (11). Also, a systematic review was done by Biessels and et al. (12). This systematic review examines the incidence of dementia in people with T2DM. Results showed the incidence of "any dementia" was higher in individuals with T2DM than in those without diabetes. The findings of mechanistic studies suggested that vascular disease and alterations in glucose, insulin, and amyloid metabolism underlie the pathophysiology, but which of these mechanisms are clinically relevant is unclear (12).

In the same way, Roberts and et al (13), designed a study to investigate the association of T2DM with mild cognitive impairment. Subjects aged between 70 to 89 years were selected and examined by the clinical dementia rating scale, and a neuropsychological evaluation to diagnose normal cognition, mild cognitive impairment, or dementia. Results showed the frequency of T2DM was similar in subjects with mild cognitive impairment and in subjects without mild cognitive impairment (odds ratio [OR], 1.16; 95% confidence interval [CI], 0.85-1.57). Mild cognitive impairment was associated with onset of T2DM before 65 years old, T2DM duration of 10 years or longer, treatment with insulin, and the presence of T2DM complications (13).

Roohollahi-Koshteli and et al (14) established a study to investigate the association among exact blood glucose control, cognitive values, and patients' demographic properties on 73 patients with type I and T2DM. The patients were assessed laboratory values, such as hemoglobin A1c (HbA1c), 2-hour postprandial blood sugar (2-h PPBS), fasting blood sugar (FBS), in the recent 6 months. Results showed, there was a meaningful association between recent FBS, 2h PP BS, HbA1C levels and patients' cognitive values. The findings indicated that cognitive impairment in T2DM and elderly are more than other ages (14).

In the same way, Depp and et al (15) examined associations of obesity and treated hypertension and diabetes with cognitive ability in bipolar disorder and schizophrenia. Results showed patients with bipolar disorder were less obese than those with schizophrenia. Obesity and treated hypertension were associated with sever global cognitive ability in bipolar disorder, but not in schizophrenia (15).

Moattar, Jamalnia and et al (6) examined the prevalence of cognitive impairment in patients with T2DM and its relationship with quality of life, self-management profiles, and HbA1c. This cross-sectional study was performed on 350 patients with T2DM. All the participants

completed the brief psychological, demographic, quality of life, and self-management profile questionnaires. Then, HbA1c levels were examined. The significant relationship was found between the cognitive impairment score and HbA1c level, some aspects of quality of life, and self-management profile. As the cognitive impairment score increased, quality of life and self-management profile was decreased and a decreasing trend was observed in HbA1c levels in moderate to normal cognitive impairment states (6). Also, Downer And et al (2016) studied the effect of undiagnosed diabetes on the relationship between self-reported diabetes and cognitive impairment. Participants older than 60 years old were classified as nondiabetic (n = 589), undiagnosed diabetic (n = 201), and self-reported diabetic (n = 243). The relationship between self-reported diabetes and severe cognitive impairment is underestimated when undiagnosed diabetics are not differentiated from self-reported diabetics and non-diabetics (16).

Although most studies have suggested that there is a direct relationship between cognitive impairment, Alzheimer's disease and T2DM, There were few studies that did not recognize any relationship. In the study conducted by Mac Knight and et al (17) the relationship between diabetes and incident dementia (including Alzheimer's disease and vascular cognitive impairment) investigated in a 5 years longitudinal. The study showed that despite increased recognition of the role of vascular factors in Alzheimer's disease, they did not find an association between diabetes and Alzheimer's disease (17).

## Discussion

T2DM is a complex metabolic disease that can cause severe damage to many organs (18). It has been proven that T2DM is an independent risk factor for eye, kidney and neurological diseases as well as cardiovascular diseases and cognitive impairment (12). Cognitive impairment has been stated in type 1 and T2DM, clearly, good control of blood glucose

levels shows the best current approach to stop cognitive impairment (9). Growing numbers of people are expanded T2DM, but interposition to ban and act the classic microvascular and macrovascular complications have better, so that people are living longer with the condition. The cause of dementia and cognitive impairment in people with T2DM is multifactorial (19). This review supports the result that compared healthy people with diabetes and showed reduction in cognitive function in T2DM patients. Data indicate that the brains of old people with type 2 diabetes mellitus might be susceptible to frequent and severe hypoglycemia (3). The results of the studies summarized here indicated that cognitive dysfunction should be considered as another consequence of chronic and irresponsible diabetes. They highlight the importance of measuring of cognitive function in future studies and other treatment for people with diabetes, to determine whether or not this decline can be reduced (5).

## Conclusions

Conclusions are different depending on the sampling, methods, the design of study, tests for cognition evaluation and diabetes severity.

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