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Cognitive Dysfunction in Diabetes Mellitus

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Abstract

People with diabetes mellitus type 2 will have higher rate of cognitive impairment than people that do not. Besides that, the effect of diabetes on the normal mental functions is often disregarded. This may be due to a lack of signs and standard assessment technique to measure the cognitive function of the diabetes patient. Hyperglycaemia which is common in people with diabetes has been associated with an increase in the possibility of developing Alzheimer's disease and vascular dementia in the both general public and people with cognitive impairment. It has been estimated that an individual with diabetes mellitus is 1.5 times more likely to experience cognitive dysfunction and dementia than a normal healthy individual. Alleviation of microvascular complications and hypoglycaemia is the key in treatment of DM to prevent cognitive decline.

Keywords: diabetes, cognition, age, glucose impairment, HbA1c

1. Introduction

According to the International Diabetes Federation, diabetes is one of the largest global health emergencies of the twenty-first century and is the top 10 causes of death globally [1]. Diabetes mellitus (DM) is a disease in which the human body cannot produce sufficient amount of insulin and fails to respond to the hormone insulin that will result to the abnormal increase of glucose level in the blood circulation resulting in hyperglycaemia [2]. It is a complex metabolic disorder which can damage multiple organs in the human body [3]. DM affects or even burdens individual and communities with huge economic cost and leads to a decrease in overall productivity [4]. The complications of DM, especially type 2, can be enhanced by comorbidities such as hypertension, stroke, etc. [5]. Diabetes is the leading problem of kidney failure, lower-limb amputation and also blindness among adults [6]. In Malaysia, diabetes is one of the main public health problems and is closely related to avoidable and premature death [7].

The World Health Organization (WHO) divides the DM into two major categories which are insulin-dependent diabetes mellitus (IDDM) or type 1 diabetes mellitus and non-insulin-dependent diabetes mellitus (NIDDM) or type 2 diabetes mellitus [8]. Approximately 90% of all diabetes cases in both developed and developing countries are NIDDM and can be found mostly in people more than 30 years old [9]. In type 1 DM, the pancreas cannot produce insulin, and the body has to completely rely on the synthetic insulin to reduce the glucose in the blood.

Type 1 DM is common in children, teenager as well as young adult [10]. DM can lead to complications such as diabetic nephropathy, diabetic retinopathy, ischaemic heart disease and many more [11]. The number of people with type 2 DM is increasing in every country with 79% of people with DM living in low- and middle-income countries [12].

1.1 Global and Malaysian scenario of type 2 DM

Some 425 million people worldwide, or 8.8% of adults, are estimated to have diabetes [13]. About 79% lives in low- and middle-income countries. If these trends continue, by 2045, some 629 million people will have diabetes [13]. The estimated population of Malaysia in 2018 is 32.4 million [14]. There were almost 3.49 million cases of diabetes in Malaysia in 2017 [15]. The percentage of population aged 15–64 years old (working age) increases from 69.6% in 2017 to 69.7% in 2018. The percentage of 65 years and over (old age) population increases from 6.3 to 6.5% for the same period [14]. The number of deaths was divided into two groups of ages which are age between 30 and 69 years old as well as ages more than 70 years old. For example, the number of diabetes deaths for female ages more than 70 years old was 1260 people compared to 1070 for males [13].

2. Cognitive function

Cognitive function can be defined as mental process (cerebral activities) that lead to the gaining of knowledge which allows people to carry out their daily life activities [16]. Cognitive functions are mainly related to remembering, solving problems, making decision and understanding the language, problems or even issues like personal issues and health issues, focus, attention and others [2]. It also can be defined as memory which is tested by the stimuli either spoken or presented using another talking format or talking memory [17]. Moreover, it can be related to the large spectrum of cognitive capability among the middle- and old-aged group of people, which are having dementia as well as maintaining normal physiological function [18].

2.1 Relationship of cognitive function with type 2 DM

Cognitive impairment is a type of disorder which has not been studied and explored as the complications of DM. At the same time, the association of DM with cognition is well acknowledged. The meta-analysis shows small to moderate performance decline in persons with diabetes relative to nondiabetic controls in each domain examined. The motor function is largely affected, while attention/concentration is affected minimally [19]. Another study shows that people with type 2 DM will have higher rate of cognitive impairment than people that do not have DM [20]. Besides that, the effect of diabetes on the normal mental functions is often disregarded. This may be due to lack of signs and standard assessment technique to measure the cognitive function of the diabetes patient [21]. Hyperglycaemia which is common in people with diabetes has been associated with an increase in the possibility of developing Alzheimer's disease and vascular dementia in both the general public and people with cognitive impairment [22]. It has been estimated that an individual with DM is 1.5 times more likely to experience cognitive dysfunction and dementia than a normal healthy individual [23].

Elderly people who are more than 65-year-old will have more than 20% chances to be diagnosed with both DM and impaired cognitive function [24]. Type 2 DM has been associated with few cognitive impairments such as decreases in

psychomotor speed, processing speed, visual retention, attention, concentration and many more. It is understood that more significantly hyperglycaemia, vascular disease, hypoglycaemia and insulin resistance affect cognitive decline, but the exact pathophysiological mechanisms not of cognitive decline in diabetes are unclear [3]. The causes of cognitive decline in diabetes may be the direct effect of the chronic hyperglycaemia on the brain regions, blood lipid, blood pressure, hypoglycaemia and others [25].

2.2 Duration of DM and cognitive impairment

Several studies have studied about the linkage of DM with cognitive decline in elderly population. A perspective (over 20 years) cohort study in the USA with mid-age (mean age 58) diabetic patient reported that DM in the midlife was related to a significant increase in cognitive impairment. This study included 13,351 black and white adults aged 48–67 years old, and their cognitive function was examined using three cognitive tests, which are the delayed-word-recall test (DWRT), the digit substitution test (DSST) of Wechsler Adult Intelligence Scale-Revised (WAIS-R) and the word fluency test (WFT). The study also reported that a patient with poorly controlled DM might have bigger cognitive disorder than well-controlled ones and longer duration of DM will have increased chances of late-life cognitive disorder [26].

A cross-sectional study was conducted on 57 patients having type 2 DM. The result shows that patients with type 2 DM had low grades in the cognitive testing and poor performance in different cognitive function tasks which include the verbal relations, visual reasoning, short-term memory test and many more. Cognitive function is impaired more with the untreated DM patient than the treated group [25]. Cognitive dysfunction is nonlinearly related to the duration of diabetes. However, cognitive decline is more prominent when the duration of DM is more than 5 years and presence of hypertension which further increases the risk of cognitive impairment [21]. The patients having diabetes showed poor performance in the tests of recent memory, repetition and attention, as compared to the control group and DM, and the people with long history of DM are more at risk of cognitive decline [27]. It is concluded that cognitive function of diabetes type 2 patients should frequently be tested. This is because the duration of disease can be related with the decrease in cognitive function. As duration increases, impairment also increases [28].

2.3 Influence of age and cognitive impairment

A prospective study is done to observe and determine the impact of DM on the cognitive function impairment in the oldest of the old participants. The study was conducted using prospective population method. They have chosen approximately 599 participants with the respond rate of 87% with the age ranges from 85 to 90 years old. The memory function test does not show any differences between both diabetic and nondiabetic participants. Cognitive function of diabetic participants is affected when the time and speed test has been conducted [29].

The results of another research show that diabetic patients more than 65 years old have higher chances to be associated with impaired cognitive function [24]. Besides that, one more study was conducted that is related to assessing the status of cognitive function in people that have DM. The chosen patients were assessed by using MMSE and 3MS (the modified mini-mental state examination). The scores for both assessments were 30 and 100, respectively. At the same time, the relationships of age, gender and duration of diabetes and HbA1c among the DM with 3MS will also be assessed. The results of this study were diabetic patients have lower

MMSE and 3MS than nondiabetic patients. This mean cognitive function will be reduced as the age increases and when having DM [30].

The uncontrolled DM which is one of the risk factors for cognitive impairment and dementia especially in Alzheimer patients. Therefore, controlling DM can reduce the possibility to get cognitive impairment and Alzheimer disease [5].

2.4 Association between duration of DM and age towards cognitive impairment

According to a homogenous cohort study on the community-dwelling women in 11 US states. This study focusses on women that live in the community which are on their own compared to living in nursing or old folk home. The result of this research was participants (women) with type 2 DM had lower mean score in all the tests conducted than women without DM. At the same time, when duration has been diagnosed with DM and insufficiency in pharmacological treatment, it can worsen or cause increment in cognitive impairment. One of the limitations for this research is self-reporting regarding diabetes diagnosis [31].

Meanwhile, another study was done regarding the cognitive impairment in diabetic patients with special references to age of onset, duration and also control of diabetes. The study was conducted in diabetic patients that came to the medicine inpatient and outpatient departments and diabetic clinic of SSKM Hospital, India. It is used to calculate the mean effect of sugar control after a 6-month period. The result of this study was cognitive impairment has a relationship with diabetes. The cognitive function that usually affected were recognition, fluency and immediate memory power of the patients. Control of DM can help in improving cognitive function of the patients. Other habits such as smoking, poor control of sugar intake as well as life style can enhance the effect of cognitive impairment [32].

A cross-sectional study was conducted which is related to prevalence and predictors of cognitive dysfunction in type 2 DM population of Punjab, India. The study involves 516 type 2 DM participants that attended the endocrinology outpatient department of the Government Medical College and Hospital, Patiala, Punjab, India. The result of this study shows that many of diabetic participants that are living in Punjab, India, remain undiagnosed with cognitive impairment during their life. Cognitive impairment in diabetic participants is independently influenced by duration of diabetes, age of the patients and other complications besides diabetes such as hypertension and others [33].

2.5 HbA1c control and cognitive decline

HbA1c is recommended to be used to identify the people at risk of developing diabetes as well as to diagnose diabetes. It is the most important biomarker for the management of blood glucose control in individuals with already diagnosed diabetes [34]. It is also a strong predictor for ensuing diabetes, because it incorporates the average blood glucose level over the last 2–3 months [35] and has better reliability than fasting or postprandial blood glucose test [36]. The cohort studies conducted in middle-aged populations show that the cognitive decline in people with diabetes is significantly faster than those with normal blood glucose levels [26, 37]. The study also reported that there is no significant difference in cognitive decline in people with prediabetes than in those with normal blood glucose levels [13]. On the contrary, the other study reported significantly faster cognitive decline among people with prediabetes than those with normal HbA1c levels [26]. The longitudinal study done reported significant longitudinal associations between HbA1c levels, diabetes status and long-term cognitive decline [38].

3. Cognitive deficits in patients with type 1 and type 2 DM

The cognitive domains that were negatively affected have been identified in patients with type 1 and type 2 DM with strong supporting data (**Table 1**).

The cognitive domains that were negatively affected have been identified in patients with type 1 and type 2 DM with less supporting data (**Table 2**).

3.1 Physiological pathways linking diabetes and cognition

The link between diabetes and cognitive impairment was first reported in 1922 [58]. The exact physiologic pathways linking the two conditions remain unclear. The hypothetical mechanisms include which is related to cerebrovascular complications, neuronal glucose processing and frequent episodes of hypoglycaemia [3, 59, 60]. The diabetic patients are more prone to develop comorbid cardiovascular disease, which is itself predictive of cognitive decline through cerebrovascular events and other pathways [61].

3.2 Treatment strategy

There are some complications of type 2 DM that affect the brain; it is believed that diabetes treatment may have beneficial effects on cognition. Three different trials reported that intensive glycaemic control alleviate microvascular complications but does not alleviate macrovascular complications in geriatric patients with long-duration of type 2 diabetes and high cardiovascular risk [62–64]. The intensive treatment of type 2 DM leads to hypoglycaemia which may contribute to cognitive decline and eliminate the benefits of intensive treatment [63, 65, 66]. Hypoglycaemia is more common in intensive glycaemic control than in standard glycaemic control [67].

Type 1 DM	Type 2 DM
Slowing of information processing [39–42]	Psychomotor speed [43]
Psychomotor efficiency [39, 40, 44]	Memory
Attention [42]	Working memory [45, 46]
Visuoconstruction [42]	Verbal memory [47]
	Immediate recall
	Delayed recall [31]
	Executive function [43, 45, 46]

Table 1.
Cognitive domains affected by type 1 and type 2 DM (with strong supporting data).

Type 1 DM	Type 2 DM
Memory [44]	Verbal fluency [43, 48]
Motor speed [41, 49–51]	Complex motor function [43]
Vocabulary [44, 52–54]	Processing speed [47]
General intelligence [53, 54]	Attention [55]
Visual perception	Depression [45, 56]
Motor strength [51]	
Executive function [49, 57]	

Table 2.
Cognitive domains affected by type 1 and type 2 DM (with less supporting data).

4. Conclusion

DM is an important risk factor along with other diabetic complications for cognitive decline, which leads to loss of independence and nonadherence to medication and results in high healthcare cost. It is still controversial how early the age of cognitive impairment is, although there is enough documented links between diabetes and cognitive function. The standard glycaemic control is better than intensive glycaemic control in the prevention of cognitive decline. The challenge for treatment is to maintain the cognitive function by reduction of hypoglycaemic events.

Conflict of interest

There is no conflict of interest among the authors.

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