

Mild Cognitive Impairment among Type 2 Diabetics Attending Zagazig University Hospitals

Thesis

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List of Abbreviations

Abb.	Full term
<i>AD</i>	<i>Alzheimer's Disease</i>
<i>APs</i>	<i>Amyloid Plaques</i>
<i>BMI</i>	<i>Body Mass Index</i>
<i>CAD</i>	<i>Coronary Artery Disease</i>
<i>CASI</i>	<i>Cognitive Abilities Screening Instrument</i>
<i>CI</i>	<i>Cognitive Impairment</i>
<i>CKD</i>	<i>Chronic Kidney Disease</i>
<i>CVD</i>	<i>Cardiovascular Disease</i>
<i>DASH</i>	<i>Dietary Approaches to Stop Hypertension</i>
<i>DCCT/EDIC</i>	<i>Diabetes Control Complications Trial / Epidemiology of Diabetes Interventions and complications</i>
<i>DHA</i>	<i>Docosahexaenoic acid</i>
<i>EMR</i>	<i>Eastern Mediterranean Region</i>
<i>EPA</i>	<i>Eicosa-pentaenoic Acid</i>
<i>ERSD</i>	<i>End Renal Stage Disease</i>
<i>HAAS</i>	<i>Honolulu Asia-Aging Study</i>
<i>Hb a1c</i>	<i>Hemoglobin a1c</i>
<i>IDF</i>	<i>The International Diabetes Federation</i>
<i>LDL</i>	<i>Low Density Lipoprotein</i>
<i>MCI</i>	<i>Mild Cognitive Impairment</i>
<i>MEdi</i>	<i>Mediterranean diet</i>
<i>MI</i>	<i>Myocardial Infarction</i>
<i>MIC</i>	<i>Microalbuminuria</i>
<i>MMSE</i>	<i>Mini-Mental Status Examination</i>
<i>MoCA</i>	<i>The Montreal Cognitive Assessment</i>

List of Abbreviations (cont...)

Abb.	Full term
<i>MUFA</i>	<i>Mono-unsaturated Fatty Acids</i>
<i>NeTs</i>	<i>Neurofibrillary Tangles</i>
<i>PAD</i>	<i>Peripheral Artery Disease</i>
<i>PUFA</i>	<i>Poly-unsaturated Fatty Acids</i>
<i>PVD</i>	<i>Peripheral Vascular Disease</i>
<i>ROS</i>	<i>Reactive Oxygen Species</i>
<i>T2DM</i>	<i>Type 2 Diabetes Mellitus</i>

INTRODUCTION

The global number of people with diabetes is estimated to increase from 171 million in 2000 to 366 million by 2030 (*WHO, 2016*).

The prevalence was highest in the Eastern Mediterranean region (EMR) increasing from 5.9% (6 million) in 1980 to 13.7% (43 million) in 2014. Regarding diabetes-related deaths, 43% occurred before the age of 70, with the highest proportion occurring in low- and middle-income countries (*WHO, 2016*).

The International Diabetes Federation (IDF) listed Egypt among the world top 10 countries in the number of patients with diabetes (*IDF, 2015*).

In Egypt, the prevalence of diabetes is around 15.6% between 20 and 79 years of age, with an annual death of 86,478 related to diabetes. In 2013, the IDF estimated that 7.5 million individuals have diabetes and around 2.2 million have pre-diabetes in Egypt. Furthermore, reports indicate that 43% of patients with diabetes and most patients with pre-diabetes in Egypt are likely undiagnosed. It is alarming that diabetes prevalence in Egypt has increased rapidly within a relatively short period from approximately 4.4 million in 2007 to 7.5 million in 2013. It is expected this number will jump up to 13.1 million by 2035 (*IDF, 2013*).

Diabetes mellitus not only causes somatic complications but also may result in accelerated cognitive dysfunction. Dementia and cognitive decline are among the most common and most feared conditions of old age, making the identification of modifiable risk factors for dementia, an urgent public health priority (*Wilson et al., 2006*). So diabetic patients may be particularly vulnerable to developing mental health disorders because diabetes is considered one of the most psychologically and behaviorally demanding chronic medical conditions (*Lisi et al., 2010*).

By 2050, 115 million people worldwide are expected to have some form of cognitive impairment including mild cognitive impairment and dementia with the increase of the aging population.

Many studies have suggested that demographic factors, lifestyle, functionality status, and chronic diseases (e.g. diabetes mellitus, hypertension and cardiovascular disease) are associated with cognitive impairment (*Solfrizzi et al., 2011*).

Cognitive function is of particular importance because of its impact on self-care and quality of life. Although patient-centric management strategies are recommended for everyone, some age-related conditions are not well understood and their impact on diabetes management in the aging population is still evolving. Traditional diabetes management strategies stress the role of the patient as an important member of the diabetes

management team and focus on the selfcare education needed to care for diabetes and related syndromes. Thus, the presence of cognitive dysfunction is an important condition to recognize as it interferes with patients' participation in their diabetes management (*Diabetes Care, 2017*).

Cognitive dysfunction is a broad term that includes many domains, such as memory, learning, mental flexibility, attention, and executive function (*Diabetes Care, 2017*).

Mild cognitive impairment also puts the patient at risk for delirium, which is a sudden worsening in the cognitive function in the presence of acute medical illness. For patients with diabetes, executive functions are particularly important as they involve behaviors, such as insight into a particular problem, problem-solving, judgment, stopping or changing old habits, and starting new habits. All of these behaviors are important when patients are asked to do complex tasks such as matching insulin dose with carbohydrate content, predicting the impact of physical activity on blood glucose, or even recognizing and treating hypoglycemia appropriately (*Diabetes Care, 2017*).

AIM OF THE WORK

- To assess the relation between mild cognitive impairment and type 2 diabetes.
- To identify risk factors related to mild cognitive impairment.

REVIEW OF LITERATURE

Diabetes mellitus is a metabolic disorder characterized by chronic hyperglycemia with disturbances in the metabolism of carbohydrates, lipids and proteins resulting from defects in insulin secretion, insulin action or both (*WHO, 2013 & IDF, 2013*).

There are two major clinical subtypes of diabetes: insulin-dependent diabetes (diabetes type 1), which accounts for 5–10% of total diabetic patients, and non-insulin-dependent diabetes (diabetes type 2), which accounts for the majority of the remaining diabetic patients (*WHO, 2013*).

In addition, there are other types such as gestational diabetes which refers to glucose intolerance with onset or first recognition during pregnancy., monogenic diabetes which is a rare disorder caused by genetic defects of beta cell function that typically presents in young people (<25 years of age). It's noninsulin dependent and familial with an autosomal dominant pattern of inheritance, cases associated with disease of the exocrine pancreas (cystic fibrosis) and cases induced by drug exposure (such as glucocorticoids, medications to treat HIV/AIDS, and atypical antipsychotics) (*Amed et al., 2016*).

Type 2 Diabetes Mellitus & its complications

Type 2 of diabetes (T2DM) is characterized by disorders of insulin action and insulin secretion. Both are usually present at the time that this form of diabetes is clinically manifest (*WHO, 2016*).

Insulin is a protein (hormone) synthesized in beta cells of pancreas in response to various stimuli such as glucose, sulphonylureas, and arginine however glucose is the major determinant (*Joshi et al., 2007*).

Type 2 diabetes is a progressive disease, it begins as pre-diabetes which can be defined by the following lab values: fasting blood sugar level ranging from 100-125 mmol/L and an HbA1c of 5.7–6.4% (39–46 mmol/mol) (*ADA, 2016*).

It is frequently undiagnosed for many years because the hyperglycemia is often not enough to provoke symptoms of diabetes (*WHO, 2014*).

Therefore the onset of T2DM is often silent and many years may pass before diagnosis. The estimated time is at least 4–7 years and consequently 30–50% patients may remain undiagnosed (*WHO, 2016*).

Diabetes is a chronic disease if not detected, managed and controlled it may lead to disability, poor quality of life and

a high mortality burden (*Agyemang et al., 2015*). Diabetes is considered the 7th leading cause of disability worldwide (*Fincke et al., 2005*). Age-standardized mortality rates reach up to 140 per 100,000 population in the EMR region (*WHO, 2016*).

Coexisting disorders including obesity, hypertension, and dyslipidaemia contribute to the severity of type 2 diabetes (*UKPDS, 1998*). Macro- and microvascular diabetic complications are mainly due to prolonged exposure to hyperglycemia, clustering with other risk factors such as arterial hypertension, dyslipidemia as well as genetic susceptibility (*Paneni et al., 2013*).

Macrovascular complications are mainly represented by atherosclerotic disease and its manifestations, such as peripheral vascular disease (PVD), stroke, and coronary artery disease (CAD). Microvascular diseases include retinopathy with potential blindness, nephropathy that may lead to renal failure and neuropathy with risks of foot ulcers, amputation, charcot joints and features of autonomic dysfunction including sexual dysfunction. Diabetes also affects the heart muscle, causing both systolic and diastolic heart failure (*Paneni et al., 2013*).

Early dysglycemia caused by insulin resistance or impaired insulin secretion is responsible for functional and structural alterations of the vessel wall culminating with