The role of glycosylated hemoglobin in the development of Alzheimer's disease in elderly patients with uncontrolled diabetes mellitus type 2 in Baquba city

El papel de la hemoglobina glicosilada en el desarrollo de la enfermedad de Alzheimer en pacientes ancianos con diabetes mellitus tipo 2 no controlada en la ciudad de Baquba

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Abstract

Background: the link between Alzheimer's disease and diabetes continues to grow stronger. Many studies have shown an association between Diabetes mellitus and cognitive function disorders. glycosylated hemoglobin has been proposed as biomarker has a great potential to predict dementia and cognitive decline in uncontrolled Diabetes. Research suggests that poorly controlled Diabetes can impact the Cognitive functionality of the patients in a negative way. Further, based on the literature the Alzheimer's type Dementia is found to be linked with the uncontrolled type 2 Diabetes Mellitus This study aims to assess the role of glycosylated hemoglobin in the development of Alzheimer's disease in elderly patients with uncontrolled type 2 Diabetes mellitus. **Methods**: Twenty-six type 2 diabetic patients and twenty-six control healthy subjects were enrolled in this study. Glycosylated hemoglobin was measured to all of them, twice during the study period and the mini-mental status examination was determined at the beginning and the end of the study. **Results**: case-control study for 52 patients with dementia, 26 patients with Diabetes mellitus and 26 normal patients, mean age of 68 ± 2 years old, with diabetic duration 3 ±1 years. The first examination of diabetic patients shows 85% of them with normal symptoms of dementia, while 11% moderate and 4% mild symptoms. After 2nd examination after average 2-3 years, show 46% normal, 31% mild, 15% moderate and 8% severe symptoms. There was a significant difference between HbA1c first and HbA1c second evaluation between diabetic and normal patients' group. In the first and second evaluation HbA1c was higher in the diabetic group when compared with normal group. **Conclusion**: During both periods of evaluation, there was a significant difference between HbA1c in diabetic and normal patients' group with Alzheimer's disease in elderly patients with uncontrolled diabetes mellitus type 2.

Keywords: glycosylated hemoglobin, Alzheimer's disease, elderly patients, uncontrolled diabetes mellitus type 2, Baquba city.

Resumen

Antecedentes: el vínculo entre la enfermedad de Alzheimer y la diabetes sigue fortaleciéndose. Muchos estudios e investigaciones han encontrado una asociación entre la diabetes mellitus y los trastornos de la función cognitiva; otros aprobaron que la hemoglobina glicosilada pueda usarse como marcador predictivo de demencia en pacientes diabéticos. Hay muchas investigaciones que discuten las complicaciones de la diabetes y lo único que puede empeorar estas complicaciones es la pérdida de memoria, especialmente en pacientes de edad avanzada. El objetivo de este estudio es explicar el papel de la hemoglobina glucosilada en el desarrollo de la enfermedad de Alzheimer en pacientes de edad avanzada con diabetes mellitus no controlada tipo 2. **Métodos**: en este estudio participan veintiséis pacientes diabéticos y veintiséis sujetos sanos control. Se midió la hemoglobina glicosilada a todos ellos dos veces / período de estudio y el mini examen del estado mental se aplica al principio y al final del estudio también. Resultados: estudio de casos y controles para 52 pacientes con demencia, 26 pacientes con diabetes Mellitus y 26 pacientes normales, edad media de ellos 68 ± 2 años, con duración diabética 3 ± 1 años, primer examen de pacientes diabéticos muestra 85% de ellos con síntomas normales de demencia mientras que 11% síntomas moderados y 4% síntomas leves, luego después del segundo examen después de un promedio de 2-3 años muestran 46% síntomas normales, 31% leves, 15% moderados y 8% severos. Hay una diferencia significativa entre la primera revisión de HbA1c y la segunda revisión de HbA1c en el grupo de pacientes diabéticos y normales, la media de la primera revisión de HbA1c en el grupo de diabéticos es mayor que la media en el grupo normal y también la media de la segunda revisión de HbA1c en el grupo de diabéticos es mayor que la media. en grupo normal. Conclusión: Diferencia significativa entre el primer control de HbA1c y el segundo control de HbA1c en el grupo de pacientes diabéticos y normales con enfermedad de Alzheimer en pacientes ancianos con diabetes mellitus tipo 2 no controlada.

Palabras clave: Hemoglobina glicosilada, Enfermedad de Alzheimer, Pacientes de edad avanzada, Diabetes Mellitus tipo 2 no controlada, Ciudad de Baquba.

Introduction

Diabetes mellitus is a common, well-known disease and it leads to many known serious complications due to microvascular and macrovascular changes. Patients with type 2 diabetes mellitus have also been found to have cognitive impairment and decrease in psychomotor speed[1] frontal lobe/executive function[2], processing speed, verbal memory[3], working memory[4], immediate recall, delayed recall[5], visual retention[6], verbal fluency and attention[7]. Type 2 diabetic patients also have an increased incidence of Alzheimer's disease and an increased incidence of vascular dementia[8]. Recently, it has been suggested that Alzheimer's disease is a form of diabetes that primarily affects the brain[9]. Alzheimer's is a kind of dementia that origins difficulties with recall, thinking, and performance. Symptoms frequently progress gradually and get poorer over time, becoming severe sufficient to affect everyday responsibilities[10]. Type 2 Diabetes mellitus (DM2) plus Alzheimer's disease (AD) are age-linked disorders, together described by high occurrence and prevalence with elderly[11]. 1% increase glycosylated hemoglobin A (HbA1c) value was associated with a significant decrease in test presentation and recall score in diabetes patients[12]. In diabetic patients, an inverse association between serum HbA1c and occupied memory, decision-making functioning, knowledge, and compound psychomotor presentation, support the theory that an insufficient glucose regulator may be related to deteriorating cognitive job[13]. Poor glycemic control in older people with DM2, and history of hypoglycemia episodes are significantly correlated with respect to cognitive decline[14]. This study aims to assess the role of glycosylated hemoglobin in the progress of Alzheimer's disease in aging patients with uncontrolled type 2 Diabetes mellitus.

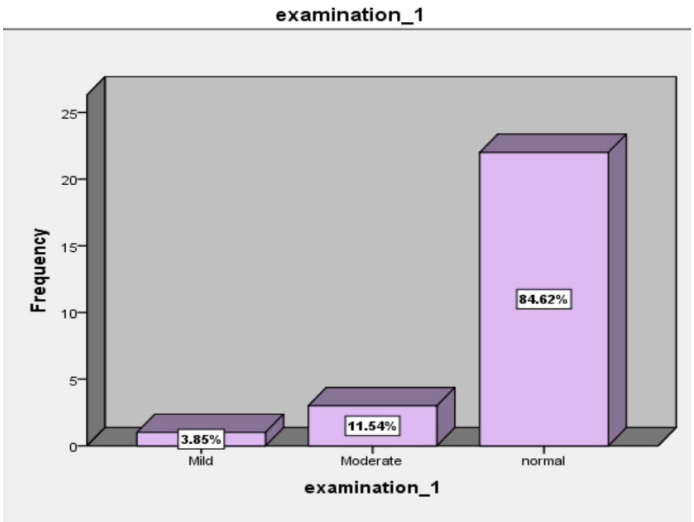
Methods

In this study fifty-two persons were enrolled in Baquba Teaching Hospital during the period between 2017 to 2019. Twenty-six of them were diagnosed with type 2 Diabetes mellitus throughout the past 5 years (diabetic group), some of them did not take any medicine, some took a mixture of herbs and drugs, and others took medicine intermittently. Twenty-six non-diabetic persons participated in this study as control (control group). The age group of both diabetic and control group was between 65-72 years of age. The study information form included age, sex, socio-economic class, marital status, living conditions, duration of diabetes and diabetes complications like retinopathy, neuropathy nephropathy, if they on insulin, oral hypoglycemic agents, herbs or any medicine, family history of diabetes and history of other diseases. All subjects were fully neurologically examined, the Mini-Mental State Exam (MMSE) was applied to diagnose Alzheimer's disease at the beginning of the study and after two years. Glycosylated hemoglobin was measured two times in two years period by using COBAS INTEGRA 400 plus analyzer.

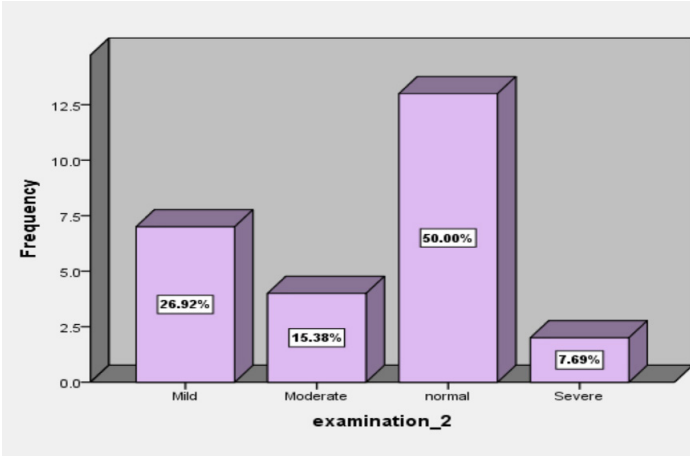
Results

Case-control study for 52 patients with dementia, 26 patients have Diabetes mellitus and 26 normal patients, mean age of them 68±2 years old, with diabetic duration of 3±1 years. The first examination of normal patients shows 85% of them with normal symptoms of dementia while 11% moderate and 4% mild symptoms, then after 2nd examination after an average of 2-3 years show 50% normal, 27% mild, 15% moderate and 8% severe symptoms. As shown in figure 1.

Figure 1. Distribution of symptoms of normal patients with dementia.

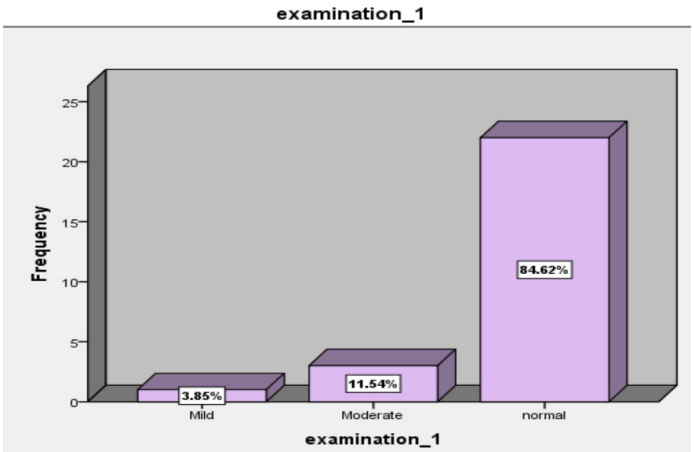


A. First examination of normal patients.
B. Second examination of normal patients

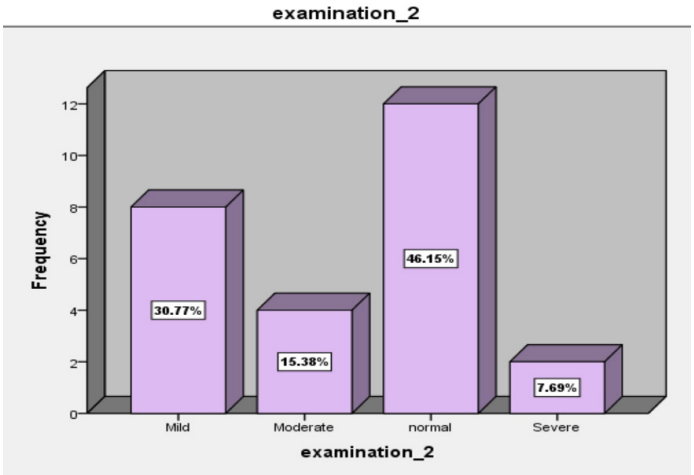


The first examination of diabetic patients shows 85% of them with normal symptoms of dementia while 11% moderate and 4% mild symptoms, then after 2nd examination after an average of 2-3 years show 46% normal, 31% mild, 15% moderate and 8% severe symptoms. As shown in figure 2.

Figure 2. Distribution of symptoms of diabetic patients with dementia



A. First examination of diabetic patients.
B. Second examination of diabetic patients.



According to Table 1, there is a significant difference between HbA1c first checkup and HbA1c second checkup in diabetic and normal patients' group, the mean of HbA1c first checkup in the diabetic group more than the mean in normal group and the mean of HbA1c 2nd checkup in the diabetic group more than the mean in the normal group. While it is no difference between diabetic and normal patients in the first and second examination of dementia symptoms.

Table 1. Statistical differences between diabetic and normal patients in HbA1c (first and second checkup) and examination (first and second).

	group	N	Mean	T	P-value
HbA1c first checkup	diabetic	26	7.0538	20.175	**0.0001**
	normal	26	4.7654		
HbA1c second checkup	diabetic	26	7.2000	21.663	**0.0001**
	normal	26	4.7346		
Examination 1	diabetic	26	1.27	0.0001	1.000
	normal	26	1.27		
Examination 2	diabetic	26	1.85	0.142	0.89
	normal	26	1.81		

P ≤0.05 (significant). Indicate the units of serum HbA1c

Discussion

Numerous studies show the association between Diabetes mellitus (DM) and Cognitive Diminishing across the world under changed geographical environments[15,16]. Type 2 Diabetes mellitus associated with multiple complications including cognitive decline and brain aging[17]. Diabetes mellitus (DM) is globally one of the key disease burdens, with about 6 million newly diagnosed patients every year. DM prevalence differs for numerous age groups. 15% of old age (more than 80 years old) have DM and 12% of patients in the age group 65-70 years old. The evidence shows a positive association between Diabetes mellitus and Cognitive deterioration. Obviously, period of Diabetes, uncontrolled Diabetes and amount of hypoglycemic incidents are powerfully associated with Cognitive deterioration[18]. Based on the significant results of this study, HbA1C as a biomarker seem to have great clinical application to predict Dementia and Cognitive decline in Diabetic subjects. HbA1C was used to describe the control of DM and we planned the same for guessing the Cognitive and Memory deterioration. Here is even less research investigating the relationship between HbA1c and cognitive decline to date. Many studies have been restricted to individuals diagnosed with diabetes[19,20], while others included both diabetics and non-diabetics with stratification by diabetes diagnosis[21,22]. Prior studies have found more consistent associations between blood glucose levels and decline in other domains of cognition, such as processing speed and executive function, compared to decline in memory[21]. Only one other study adjusted for attrition[21], and none adjusted for selective survival; however, since our use of IPWs did not qualitatively change results, bias due to selective survival and attrition may be small. Additionally, our analyses included all participants with available data, regardless of baseline cognitive status. This approach has the advantage of allowing us to identify the long-term consequences of diabetes-related processes more accurately. Possible biological mechanisms linking T2DM and cognition include chronic hyperglycemia as well as hyperinsulinemia and functional insulin deficiency in the brain. In addition, some risk factors for dementia, such as severe hypoglycemic events and depression, are more common in individuals with T2DM and could explain the association. This study lends support to the hypothesis that chronic hyperglycemia is a key pathway linking diabetes and memory decline, most likely via microvascular injury. It is possible that other mechanisms contribute to the explanation of the diabetes-memory relationship, and they may link diabetes with other domains of cognition. Each of these proposed mechanisms could affect cognitive decline and dementia via either contributing to Alzheimer's disease pathogenesis or vascular disease. Thus, we cannot discern whether HbA1c is associated with memory loss in our study because of chronic hyperglycemia influencing vascular disease or AD pathology. One main limitation to this study is the lack of assessment of many important domains of cognition, other than memory. Additionally, we cannot distinguish the cause of memory decline, e.g., Alzheimer's disease versus vascular disease. Our measure of diabetes status is self-reported physician diagnosis and therefore could suffer from bias if individuals cannot accurately report whether they have been diagnosed with diabetes. However, we excluded people whose HbA1c levels were inconsistent with their self-reported diabetes status[23].

Conclusion

A significant difference was found in both firs and second evaluation between HbA1c in diabetic and normal patients group Alzheimer's disease in elderly patients with uncontrolled Diabetes mellitus type 2.

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