Original Article

Effect of HBA1C on Cognitive Skills in Type 2 Diabetic Patients Received at Liaquat University Hospital

Suhail Ahmed Almani, Shafaq Nazia, Muhammad Iqbal Shah, Madiha Abbasi, Santosh Kumar, Zohaib Feroze

ABSTRACT

OBJECTIVE: To determine the effect of HbA1c on cognitive skills of type 2 diabetic patients received at Liaquat University Hospital, Jamshoro.

METHODOLOGY: The retrospective Cohort study was conducted on 278 patients received at Liaquat University Hospital, Jamshoro from September 2019 to March 2020. Sampling technique was non probability, consecutive. The inclusion criteria were both genders age more than 18 years and diabetes mellitus type 2 while the exclusion criteria were other causes of cognitive impairment including thyroid disease, psychiatric illness, alcohol intake, smoking, dementia, delirium, dyslipidemia, ischemic heart disease, stroke, anemia, and pregnancy. A proforma was used to collect data including Hemoglobin A1c and score obtained on General Practitioner Assessment of Cognition Scale. Analysis was done using SPSS 20. This study was funded by the authors.

RESULTS: About 55.76 % participants were males. Mean [SD] age was 54.7 [5.4] years, diabetes duration was 8.7 [5.2] years. Baseline HbA_{1c} ranged from 4.1% to 13.2%. A number of 96 patients (34.53%) were cognitively impaired as assessed by General Practitioner Assessment of Cognition Scale. Out of these, 79 patients (82.29%) had elevated HbA1c

CONCLUSION: Significant association was seen between elevated hbA1c and cognitive impairment in patients with type 2 diabetes mellitus received at medical wards of Liaquat University Hospital, Jamshoro.

KEY WORDS: HBA1C (Hemoglobin A1c), Type 2 Diabetes Mellitus, Cognitive Function

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INTRODUCTION

Type 2 Diabetes mellitus is a metabolic condition characterized by persistent hyperglycemia. It results from deficiency of insulin or reduced tissue sensitivity to action of insulin. The resultant high level of blood sugar leads to increased thirst and urination, and leads to several complications, affecting small and large blood vessels. These complications include stroke, ischemic heart disease, neuropathy, nephropathy, retinopathy and diabetic foot amongst many others. Therefore, it is necessary to keep a good glycemic control to avoid these complications. To check the glycemic control, the level of glycosylated hemoglobin in blood or HbA1c is performed, which determines the level of average blood sugar in past 2 to 3 months[1]. It is seen that many patients with type 2 diabetes mellitus develop dementia, which is characterized by amnesia and cognitive impairment[2]. Several studies have suggested an uncontrolled diabetes mellitus as a risk factor for cognitive decline[3]. This study was conducted on type 2 diabetic patients received at Liaquat University Hospital, Jamshoro, to determine the association between uncontrolled blood sugar levels represented by elevated HbA1c with a decline in cognitive skills, which is a part of dementia. We make suggestions of future research that could help us address the challenges we may face as more people live longer with diabetes than ever before and may be worth considering the inclusion of the HbA1c value in the routine cognitive skills work-up.

METHODOLOGY

This is retrospective Cohort study using non probability and consecutive sampling technique. The measured sample size for this study is 278, for 95% of confidence interval by WHO formula

$$n = \frac{z^2 \times \hat{p}(1-\hat{p})}{\varepsilon^2}$$

The setting was medical wards of Liaquat University Hospital, Jamshoro. The duration of study was 6 months from September 2019 to March 2020. The inclusion criteria were both genders age more than 18 years, diabetes mellitus type 2 while the exclusion criteria were other causes of cognitive impairment including thyroid disease, psychiatric illness, alcohol intake, smoking, dementia, delirium, dyslipidemia, ischemic heart disease, stroke, anemia and

pregnancy. The data was collected on predesigned proforma after acquiring patient consent, both informed and verbal. The data included patient demographic, age, gender, status of type 2 Diabetes Mellitus, HbA1c value, and score obtained on General Practitioner Assessment of Cognition Scale (GPACS). Diabetes mellitus type 2 was defined as adults having fasting blood sugar of, or more than 126mg/dl, random blood sugar of, or more than 200 mg/dl, HbA1c of or more than 6.5% or patient already on hypoglycemic agents. Impaired cognition was defined as a score of 5 to 8 on General Practitioner Assessment of Cognition Scale. The data was then analyzed with the help of SPSS 20 and presented in form of tables and charts. Descriptive statistics included mean +/- standard deviation (SD) of continuous data, including age, fasting blood sugar, random blood sugar and duration of diabetes mellitus. Frequencies were calculated for categorical data including gender, HbA1c and score obtained on GPAC scale. Effect modifier was controlled by stratification of age in groups, gender (male and female) and fasting and random blood sugar levels. The post stratification chi square test was applied on categorical variables at 95% confidence interval. The p value of <0.05 was considered as statistically significant.

RESULTS

This study included a total of 278 participants, out of which 155 were males (55.76 %) and 123 were females (44.24%). Mean [SD] age of the patients was 54.7 [5.4] years, and the duration of type 2 diabetes was 8.7 [5.2] years. Baseline HbA1c ranged from 4.1% to 13.2% (Table I). A number of 96 patients (34.53%) were cognitively impaired as assessed by General Practitioner Assessment of Cognition Scale. Out of these, 79 patients (82.29%) had elevated HbA1c ranging between the 8.2 % to 12.7%.

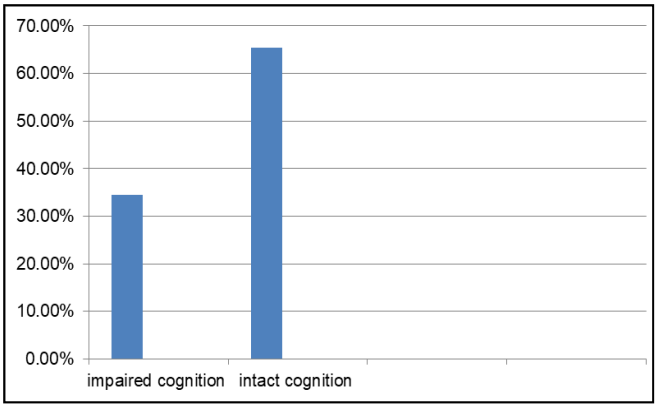
TABLE I: CHARACTERISTICS OF PARTICIPANTS

Total number of participants (n)	278
Male (n)	155
Female (n)	123
Age (years)	54.7 ± 5.4
Duration of type 2 Diabetes Mellitus(years)	8.7 ± 5.2
HbA1c range overall (%)	4.1 – 13.2
HbA1c in cognitively impaired patients (%)	8.2 – 12.7

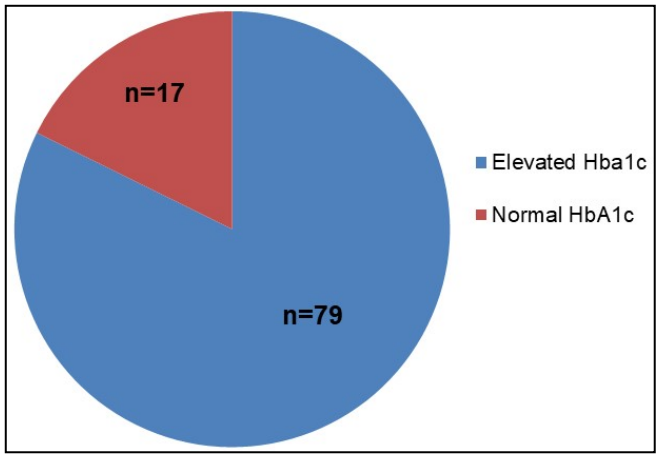
DISCUSSION

Diabetes mellitus is a global health issue. According to the International Diabetes Federation, 463 million adults between the ages of 20 to 79 years worldwide were suffering from diabetes in the year 2019. IDF also predicts that there will be 700 million people in the world with diabetes by the year 2045. As

BAR CHART I: COGNITIVE ASSESSMENT OF TYPE 2 DIABETIC PATIENTS



PIE CHART I: HBA1C IN TYPE 2 DIABETIC PATIENTS WITH IMPAIRED COGNITIVE SKILLS



compared to type 1 diabetes mellitus, the incidence of type 2 diabetes is much higher. Most of these adults belong to developing countries. But this number has already been crossed, a decade before the predicted year. This condition is not only a physical health burden but also a financial and emotional burden. Amongst numerous complications of diabetes, cognitive dysfunction is also seen in patients with type 2 diabetes mellitus[4]. Cognitive dysfunction is a component of dementia.

There are one hundred billion cells in human adult brain, called neurons. There neurons transmit and propagate information between brain cells by means of synapses and neurotransmitters. When this transmission is disrupted, it results in cognitive impairment and dementia. There are many underlying risk factors for development of cognitive dysfunction and dementia, such as old age, cholesterol[5], C reactive protein, and blood pressure. HbA1c is considered as a risk factor in such patients[6]. Higher HbA1c is associated with dementia and Alzheimer's disease[7]. There are several ways through which diabetes can affect cognition. One of which is insulin

resistance, as seen in type 2 diabetes mellitus[8].

Zheng F 2018[7] observed a trend in cognitive decline over the period of 10 years in subjects with diabetes. Moreover, increased HbA1c levels lead to a faster cognitive decline regardless of diabetes diagnosis. Memory and executive function were mostly affected during the period of 10 years; researchers argue that this decline could be related to high circulating glucose levels. By inducing amyloid accumulation, increasing microvascular disease in CNS, and by leading to depression, obesity and hyperlipidemia, diabetes can potentiate cognitive decline[9]. Yet, true mechanisms by which diabetes affects cognitive decline are unknown[10]. Early recognition of diabetes risk factors and proactive management of DM are important to prevent possible decline in cognition[11-13]. But, can the cognitive decline be slowed by having optimized HbA1c levels? To answer this question, future studies need to be completed that focus on benefits of normalized HbA1c ranges and cognition.

In a study by Cui Y 2014[14] decreased amplitude of low frequency fluctuations (possibly indicative of reduced functional connectivity) was observed in the postcentral gyrus and occipital lobe of patients with T2DM compared to controls. Interestingly, this finding was present in the absence of structural brain changes and was associated with worse memory performance and executive functioning. Disturbances of low frequency fluctuations have been observed in several additional brain areas[15,16]. In a large cross sectional study Moran C 2013[17] reported that subjects with T2DM had lower total gray, white, and hippocampal volumes. Regions with loss of gray matter include the medial temporal, anterior cingulate, and medial frontal lobes. White matter loss was found in the frontal and temporal regions.

In a study by Zhou H 2010[18], the decline in cognitive performance in T2DM was associated with a reduction in functional connectivity of the hippocampus. These are interesting observations, because patients with T2DM have an increased incidence of both Alzheimer's disease and vascular type dementia, therefore abnormal functional connectivity might constitute an early marker of subsequent cognitive decline for the patient's withT2DM.

CONCLUSION

The authors conclude that there is a significant impact of elevated HbA1c with a decline in cognitive function in patients with type 2 diabetes mellitus received at medical wards of Liaquat University Hospital, Jamshoro.

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AUTHORS CONTRIBUTIONS

Almani SA: Drafting the article and shares its expert opinion and experience in finalizing the manuscript
Nazia S: Conception and design, acquisition of data, analysis and interpretation of data
Shah MI: Acquisition of data, analysis and interpretation of data and make it suitable for final revision
Abbasi M: Contributed in conception and interpretation of data and give his expert view
Kumar S: Final proof reading, review of literature and sequencing the material as well as grammatical review.
Feroze S: Collection and acquisition of data and help in analysis and review of manuscript

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