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Original Research Article

Study to Correlate HbA1c with Attention, Executive Function and Visual Reaction Time in Type 2 Diabetes Patients

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Abstract

Aim: The aim of the present study was to correlate duration of disease with attention, executive function and visual reaction time in type 2 diabetes patients and to correlate HbA1c with attention, executive function and visual reaction time in type 2 diabetes patients.

Methods: This was a cross-sectional study done on 100 type 2 diabetes mellitus subjects of either sex under the age group of 40-60 years in the Department of Physiology for the period of two years. The subjects who are able to understand English were enrolled for the study. Written informed consent was taken and each subject was explained about the whole procedure and objective of the study.

Results: The mean age and BMI of the patients were 58.06±4.48 and 24.56+1.94 respectively. There were 55 male and 45 females in the present study. Duration of disease was positively correlated (r=0.34) with score of Digit Vigilance Test and p value statistically significant (0.016). A positive correlation (r=0.24) was also seen with Visual Reaction time and p value statistically significant (0.046). Stroop test score also shows a positive correlation (r=0.16) but without any statistical significance. HbA1c was positively correlated(r=0.56) with the score of Digit Vigilance Test and p value statistically significant (0.01). A positive correlation (r=0.36) was also seen with Visual Reaction time and p value statistically significant (0.01). Stroop test score also shows a positive correlation (r=0.16) but without any statistical significance.

Conclusion: With increase in duration of the disease and poor glycemic control, sustained attention and executive functions are declining. Also there is an increase in visual reaction time. Diabetes is a disease which requires proper self-care and monitoring. The decline in cognitive functions can affect their activities like glucose monitoring, medications or insulin injection patterns, diet and exercise timing.

Keywords: Type 2 Diabetes mellitus, Attention, Executive functions, Reaction time, HbA1c

Introduction

According to the American Diabetes Association, "Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Chronic hyperglycemia is associated with long-term multiple organ dysfunction including the eyes, kidneys, nerves, heart, and blood vessels". [1] One of the most recently discovered complications of diabetes is the progressive decrease in mental ability and cognition, in particular, there is a decrease in processing speed, verbal memory, and executive functions, whereas visuospatial, attention, semantic and language functions seem to be preserved, controlling blood glucose levels, however, has shown to help delay such affects. [2-4]

Moreover, one systemic review suggested that physical exercise decreases the diabetes-associated risk of dementia by 28% and risk of Alzheimer's disease by 45%. [5] However, other studies linked diabetes with alterations in different aspects of cognition and fatigability, regardless of blood sugar levels and disease control. [6] In 2014, a review article, including 86 articles, addressed the relationship between glucose regulation and cognitive function in type 2 diabetes mellitus (T2DM) patients and concluded that cognitive functions in type 2 diabetics without dementia are inversely correlated with levels of glycated hemoglobin. [7] And as the elevated adipose tissue is a contributor in the incidence of T2DM, a paper studying the relation between cognition and adiposity levels found that the amount of adipose tissue exceeding a certain degree in abundance would facilitate dementia progression and a decline in the overall mental status. [8]

Impaired glucose metabolism affects the micro and macrovascular systems, Kidney, Eyes & Nervous system. Neuropathy is one of the microvascular complications of diabetes and its severity of which is related to duration and degree of glycemic control which can be assessed by Blood level of glycated Haemoglobin (HbA1C). [9] Auditory and visual Reaction time is considered as an ideal tool for measuring sensory motor association and performance of an individual. There is a direct relationship between elevated levels of HbA1C & Diabetic Neuropathy has been reported in Type-II DM. [10,11]

The aim of the present study was to correlate duration of disease with attention, executive function and visual reaction time in type 2 diabetes patients and to correlate HbA1c with attention, executive function and visual reaction time in type 2 diabetes patients.

Materials and Methods

This was a cross-sectional study done on 100 type 2 diabetes mellitus subjects of either sex under the age group of 40-60 years in the Department of Physiology ICARE Institute of Medical Science and Research & Dr BC Roy Hospital, Haldia, West Bengal, India for the period of two years. The subjects who are able to understand English were enrolled for the study. Written informed consent was taken and each subject was explained about the whole procedure and objective of the study.

A detailed history taking and relevant clinical examination was done for all subjects. Following which, subjects who had hypertension, dyslipidaemia, and any diabetic complications were excluded. Also, diabetic subjects on insulin, those with visual disturbances were excluded. Fasting venous blood samples (2ml) were taken for estimation of HbA1c. HbA1c is measured in BIORAD D-10 machine using latex agglutination inhibition assay. Cognitive tests that measured performances in specific domains of interest were chosen. This includes Digit Vigilance Test (DVT) for attention and Stroop Test for executive functions. Visual Reaction Time, a measure of attention and fine motor skills were also considered.

Digit Vigilance Test: DVT was administered according to the instructions provided in the Neuropsychology Battery. [12] This test consists of numbers 1-9 arranged randomly and placed in rows in a sheet. Digits are closely packed on the sheet in 50 rows and 30 digits per row. The subject is instructed to cancel the digits 6 and 9 as fast as possible without missing targets or cancelling wrong numbers. Time taken for completion of the test forms the score and was noted using a stopwatch. Lower score indicate better sustained attention.

Stroop test: This test was administered according to the instructions provided in the Neuropsychology Battery.[12] The test consist of a paper in which the colour names BLUE, GREEN, RED, YELLOW are printed. Colour of the print occasionally corresponds with the colour designed by the word. There are 16 rows and 11 columns. The subject is instructed to read the words column wise as fast as possible. Time taken to read all the 11 columns were noted down using stopwatch. Next the subject was asked to name the colour in which the word was printed. The time taken to name all the colours in the column wise was also noted. Reading time and naming time were converted into seconds. Reading time was subtracted from naming time to get the Stoop effect score. Lower score indicates better executive functions.

Visual Reaction Time: VRT was assessed using Human Benchmark Software. [13] This software consist of a red coloured screen on the laptop monitor. The subject is instructed to focus on the screen and when the red colour changes to green colour, he/she should press the enter key on the keyboard. Five trials were given and average time was taken as the visual reaction time. Lower the reaction time better is the attention and fine motor skills.

Statistics: Data presented as Mean + Standard deviation. Pearson correlation was used to correlate duration of disease and HbA1c on attention, executive function and visual reaction time. P value <0.05 was considered statistically significant. Statistical analysis was done using Microsoft Excel 2013.

Results

Table 1: Demographic details of the study group

Parameters	Study group
Age (yrs.)	58.06±4.48
BMI (kg/m2)	24.56+1.94
Male	55
Female	45

The mean age and BMI of the patients were 58.06±4.48 and 24.56+1.94 respectively. There were 55 male and 45 females in the present study.

Table 2: Correlation between duration of disease and different tests

Test	r	p value
DVT	0.34	0.016
VRT	0.24	0.046
STROOPTEST	0.16	0.264

Here, duration of disease was positively correlated (r=0.34) with score of Digit Vigilance Test and p value statistically significant (0.016). A positive correlation (r=0.24) was also seen with Visual Reaction time and p value statistically significant (0.046). Stroop test score also shows a positive correlation (r=0.16) but without any statistical significance.

Table 3: Correlation between HbA1c and different test

Test	r	p value
DVT	0.56	0.01
VRT	0.36	0.01
STROOP TEST	0.16	0.34

HbA1c was positively correlated(r=0.56) with the score of Digit Vigilance Test and p value statistically significant (0.01). A positive correlation (r=0.36) was also seen with Visual Reaction time and p value statistically significant (0.01). Stroop test score also shows a positive correlation (r=0.16) but without any statistical significance.

Discussion

Type 2 diabetes mellitus is a common endocrine disorder [14] and is on constant rise in the world. [15] Diabetes mellitus is associated with premature mortality [16] and several complications such as neuropathy, nephropathy and cardiovascular disease. [14] It can also affect brain leading to accelerated cognitive decline and an increased risk of dementia. [17] In Cardiovascular Health Study, the prevalence of mild cognitive impairment was 19% in individuals of age > 65years and 29% in those aged >85years. [16] Cognitive decline can be seen in both type 1 and type 2 diabetes mellitus patients, but the affected domains remain distinct in these two types with executive functions, memory, learning, attention and psychomotor efficiency being more affected in type 2 diabetes mellitus patients. In diabetes patients, the executive functions are particularly important as they involve behaviours, such as insight into a particular problem, problem- solving, judgment, stopping or changing old behaviours and starting new habits, thus affecting the individual's self-care. [18]

The mean age and BMI of the patients were 58.06±4.48 and 24.56+1.94 respectively. There were 55 male and 45 females in the present study. Cognitive alterations, in the form of longer reaction times and impaired spatial planning, occur in diabetic patients. These impairments however, were unrelated to glycemic control, reflected by HbA1C levels, complications and duration of disease. [19] In a systematic analysis it has been reported that hyperglycemia is associated with impaired cognitive functions. [20] Patients with T2DM, regardless of their insulin treatment status have shown higher fatigue scores and cognitive impairment with significant prolongation of reaction times and defective spatial planning. [21]

Duration of disease was positively correlated (r=0.34) with score of Digit Vigilance Test and p value statistically significant (0.016). A positive correlation (r=0.24) was also seen with Visual Reaction time and p value statistically significant (0.046). Stroop test score also shows a positive correlation (r=0.16) but without any statistical significance. HbA1c was positively correlated(r=0.56) with the score of Digit Vigilance Test and p value statistically significant (0.01). A positive correlation (r=0.36) was also seen with Visual Reaction time and p value statistically significant (0.01). Stroop test score also shows a positive correlation (r=0.16) but without any statistical significance. It refers to the capacity to attend a task for a required period of time. Right fronto-parietal network mediates sustained attention. Executive functions tested by Stroop test indicate Response inhibition by the brain. Response Inhibition measures the ease with which a perceptual set can be shifted both to conjoin changing demands and by suppressing a habitual response in favour of an unusual one. Pre-frontal areas are essential for response inhibition. [22] Visual reaction time was tested for attention and fine motor skills. It indicates the time taken for processing of sensory stimulus by central nervous system and its execution in the form of motor response. [15]

Glucose serves as a fuel for the brain and is necessary for cognitive performances. Hyperglycemia alters the cognitive functions through a variety of mechanisms like, polyol pathway activation, increased formation of Advanced Glycated End products (AGEs), diacylglycerol activation of protein kinase C and increased glucose shunting in the hexosamine pathway. Hyperglycemia decreases the glucose

availability to the brain by impairing the transfer of glucose across the Blood-Brain-Barrier and between the intra and extracellular fluids in the brain, thus impacting cognitive performance. Even a reduction in availability of acetylcholine caused by decrease transport of glucose across the BBB is attributed to cognitive decline. [23] Diabetes Mellitus affects the peripheral nerves in the somatosensory and auditory system, slows psychomotor responses and has cognitive effects all of which may affect reaction times. [24] Some studies states that axonal degeneration of both myelinated and unmyelinated fibres, axon shrinkage, axon fragmentation, thickening of basement membrane and micro thrombi delays motor nerve conduction velocity, thus delaying the reaction time. [15]

Conclusion

Type 2 diabetes mellitus is a risk factor for cognitive impairment. In the present study, HbA1c which is a marker of chronic hyperglycemia and duration of disease are correlated with few cognitive domains like attention, executive function and reaction time. With increase in duration of the disease and poor glycemic control, sustained attention and executive functions are declining. Also there is an increase in visual reaction time. Diabetes is a disease which requires proper self-care and monitoring. The decline in cognitive functions can affect their activities like glucose monitoring, medications or insulin injection patterns, diet and exercise timing. Hence identification of cognitive impairments and their relation with Diabetes is an important step for prevention of cognitive decline.

References

1. American Diabetes Association, Diagnosis and classification of diabetes mellitus, Diabetes Care 33 (Suppl 1) (2010) S62–S69.
2. Messier C. Impact of impaired glucose tolerance and type 2 diabetes on cognitive aging. Neurobiology of aging. 2005 Dec 1;26(1):26-30.
3. Alfahadi A, Habib SS, Alharbi K, Alturki D, Alshamrani F, Bashir S. Assessment of fatigue severity and neurocognitive functions in the real setting of Ramadan in patients with type 2 diabetes mellitus. Heliyon. 2020 May 1;6(5).
4. Umegaki H, Hayashi T, Nomura H, Yanagawa M, Nonogaki Z, Nakshima H, Kuzuya M. Cognitive dysfunction: an emerging concept of a new diabetic complication in the elderly. Geriatrics & gerontology international. 2013 Jan;13(1):28-34.
5. Hamer M, Chida Y. Physical activity and risk of neurodegenerative disease: a systematic review of prospective evidence. Psychological medicine. 2009 Jan;39(1):3-11.
6. Lasselin J, Layé S, Barreau JB, Rivet A, Dulucq MJ, Gin H, Capuron L. Fatigue and cognitive symptoms in patients with diabetes: relationship with disease phenotype and insulin treatment. Psychoneuroendocrinology. 2012 Sep 1;37(9):1468-78.
7. Geijselaers SL, Sep SJ, Stehouwer CD, Biessels GJ. Glucose regulation, cognition, and brain MRI in type 2 diabetes: a systematic review. The Lancet Diabetes & Endocrinology. 2015 Jan 1;3(1):75-89.
8. Yadav, S., Gupta, D. K., Patil, P. H., Tiwari, A. ., & soni, P. . (2023). To Study the Pharmacotherapy of Diabetes Mellitus Type 2 Patient in Echo Health Care & Research Centre, Indore". Jour Med Resh and Health Sci, 6(2), 2389–2397. https://doi.org/10.52845/JMRHS/2023-6-2-1
9. Gustafson DR. Adiposity and cognitive decline: underlying mechanisms. Journal of Alzheimer's Disease. 2012 Jan 1;30(s2):S97-112.
10. Niruba R, Maruthy KN. Assessment of Auditory and Visual Reaction Time in Type 2 iabetics. Al Ameen J Med Sci. 2011;4 (3):274-79.
11. Murugan K, Shrivastava DK, Patil SKB, Lanjhiyana S, Garabadu D, Ahiwar B, et al. A Systematic Study on the Glycosylated Haemoglobin in Diabetes associated Neuropathy in Chhattissgarh Population. Der Pharmacia Sinica. 2010;1(2):122-29.
12. American Diabetes Association. Standards of Medical Care in Diabetes position statement. Diabetes Care. 2007;S8-30.
13. Rao SL, Subbakrishna DK, Gopukumar K. NIMHANS Neuropsychology Battery 2004.
14. Murray MM, Foxe JJ, Higgins BA, Javitt DC, Schroeder CE. Visuo-spatial neural response interactions in early cortical processing during a simple reaction time task: a high-density electrical mapping study. Neuropsychologia. 2001 Jan 1;39(8):828-44.
15. Biessels GJ, Van Der Berg E, Craen AJM, Gussekloo J, Westendrop RGJ. The impact of diabetes mellitus on cognitive decline in the oldest of the old: a prospective population-based study. Diabetologia (2006); 49:2015-23.
16. Sidhu J, Mittu S, Sidhu H. Visual reaction time changes in the type 2 diabetics and non-diabetics. Arch.Appl.Sci.Res.2015;7(7):59-61.
17. Yaffe TC, Gerstein HC, Williamson JD, Lazar RM, Lovato L, Miller ME et al. Relationship between baseline glycemic control and cognitive function in individuals with type 2 diabetes and other Cardiovascular risk factor. Diabetes Care feb 2009; 32(2):221-25.
18. Ruis C, Beissels GJ, Kappelle LJ, Donk M, Gorter KJ, Rutten G. Cognition in the early stages of type 2 diabetes. Diabetes care 2009; 32:1261-65.

19. Munshi MN. Cognitive dysfunction in older adults with diabetes: What a clinician needs to know. Diabetes Care 2017; 40:461-67.
20. Lasselin J, Layé S, Barreau JB, Rivet A, Dulucq MJ, Gin H, Capuron L. Fatigue and cognitive symptoms in patients with diabetes: relationship with disease phenotype and insulin treatment. Psychoneuroendocrinology. 2012 Sep 1;37(9):1468-78.
21. Geijselaers SL, Sep SJ, Stehouwer CD, Biessels GJ. Glucose regulation, cognition, and brain MRI in type 2 diabetes: a systematic review. The Lancet Diabetes & Endocrinology. 2015 Jan 1;3(1):75-89.
22. Lasselin J, Layé S, Dexpert S, Aubert A, Gonzalez C, Gin H, Capuron L. Fatigue symptoms relate to systemic inflammation in patients with type 2 diabetes. Brain, behavior, and immunity. 2012 Nov 1;26(8):1211-9.
23. Rao SL, Subbakrishna DK, Gopukumar K. NIMHANS neuropsychology battery-2004, manual. National Institute of Mental Health and Neurosciences; 2004.
24. Kodl CT, Seaquist ER. Cognitive Dysfunction and Diabetes Mellitus. Endocr Rev. 2008 Jun; 29(4):494-511.