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A COMPARATIVE STUDY OF COGNITIVE FUNCTION AND INFORMATION PROCESSING ABILITY AMONG TYPE 2 DIABETES MELLITUS PATIENTS AND HEALTHY VOLUNTEERS

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ABSTRACT: INTRODUCTION: Prevalence of Diabetes is in increasing trend worldwide particularly in south East Asian countries including India. Diabetes by itself has been implicated as an independent risk factor for the abnormalities of higher functions. **OBJECTIVES:** This study oriented towards comparison of cognitive function and information processing ability of diabetes patients with that of healthy individuals. **MATERIALS AND METHODS:** In this cross sectional prospective study 50 known type 2 diabetes mellitus individuals (Group-1) and 50 non diabetic healthy control subjects (Group-2) were selected from the outpatient clinic in a tertiary teaching hospital. Screening test was conducted for both the groups using Addenbrooks's Cognitive Examination (ACEIII) and Deary- Liewald reaction time task, a computer based test to study Simple Reaction Time (SRT) and Choice Reaction Time (CRT). **RESULTS:** The ACEIII score differ between diabetic and non-diabetic. The difference between the two group were statistically significant [$p < 0.05$] Diabetes patients took more time than normal individuals in Simple Reaction Time (SRT) [$p < 0.05$] and Choice Reaction Time (CRT) [$P < 0.05$] **CONCLUSION:** This study clearly indicates that type 2 diabetics are at increased risk of developing dementia.

KEYWORDS: Cognitive function, information processing ability, ACEIII, SRT, CRT.

INTRODUCTION: The prevalence of Diabetes is rising all over the world. India, being termed the "Diabetes capital of the world" currently has 40.9 million diabetics and is expected to rise to 69.9 million by 2025 according to the Diabetes Atlas 2006 published by the International Diabetes Federation.¹ There is a peculiar phenotype called "Asian Indian Phenotype" characterized by increased insulin resistance, greater abdominal adiposity that makes Asian Indians more prone to diabetes and its complications. Even though there is an increase in the prevalence of type 1 diabetes, it is the type 2 diabetes, which accounts for more than 90 percent of all diabetes cases.² Even though Type 2 Diabetes is associated with various vascular risk factors for cognitive dysfunction and information processing slowing, diabetes by itself has been implicated as an independent risk factor for these abnormalities of higher functions. Studies utilizing neuroimaging techniques had shown that cognitive impairment in type 2 diabetics had been associated with sub cortical ischemic changes and increased brain atrophy.³ in routine clinical care, evaluation of cognitive function in diabetics is usually not given much importance. With increasing life expectancy and increase in diabetics in India, it is pertinent to evaluate cognitive impairment in diabetics using simple screening tests.

Several screening tests have been developed to detect cognitive impairments. The most widely used and validated test is The Mini-Mental State Examination (MMSE) but it has certain limitations such as insensitivity to detect early stages of impairment and the use of simple tasks for

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language and memory functions. Addenbrooke's Cognitive Examination (ACE-III) incorporates certain key aspects of cognition without the use of specialized test equipment. It is a bedside or clinic-based test that incorporates memory, language, and visuospatial components, and adds tests of verbal fluency.⁴

One cognitive domain, which is not well covered by ACE-III, is the fluid intelligence, which is key to problem solving. There is paucity of literature in the effect of Type II diabetes on reaction time, which is widely used representative index of fluid intelligence and information processing efficiency. Fortunately, now there is a free, easy-to-use, computer-based simple and four choice reaction time task by name Deary- Liewald Reaction Time Task.⁵ This study was undertaken with the objectives to assess cognitive impairment in type 2 diabetes mellitus using Addenbrooke's Cognitive Examination (ACE-III) and to assess information processing efficiency in type 2 diabetes mellitus using Deary-Liewald Reaction Time Task.

MATERIAL AND METHODS: This study was conducted in a tertiary teaching hospital in Tiruchirappalli, Tamilnadu.

Study Design: This study was a Case Control Study, and pretested known diabetic patients under medication and Non-diabetic healthy volunteers above the age of 50 years of both sexes were selected for this study.

Sample size: The study was carried out among 50 type 2 diabetics under medication and 50 healthy volunteers of both sexes.

Inclusion Criteria: Patients with type 2 diabetes mellitus including both male and female diagnosed according to WHO criteria for the diagnosis of diabetes mellitus and healthy volunteers of same age group with educational qualification of high school level and above were included for this study.

Exclusion Criteria: People with any psychic disorder, alcoholic, tobacco users, cerebrovascular diseases, Hypertensive's and individuals under medication for any other systemic illness and any diabetics with psychoactive drugs were excluded from the study.

MATERIALS AND METHODS: A battery of 50 known type 2 diabetes mellitus individuals and 50 non diabetic healthy control subjects who are the relatives of the study subjects were selected from the outpatient clinic. A detailed history was taken from the study and control groups regarding diabetes, other co morbid conditions, investigations and past and current medication details. Detailed general and systemic examinations were done.

SCREENING TESTS:

Addenbrooks's Cognitive Examination (ACEIII): It contains 5 sub scores, each one representing one cognitive domain: viz attention/ orientation (18 points) memory (26 points), fluency (14 points), language (26 Points) and Visuospatial (16 Points). It takes between 15 and 20 min to administer and score the test. ACE-R maximum score is 100, calculated by the addition of all domains. A cut-off score < 88 confer 94 % of sensitivity and 89% specificity for dementia. And cut off <82 grant 84% sensitivity and 100% specificity for dementia.⁴ The participants were asked to answer the question in the ACE III and answers were computed and analyzed.

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The Deary-Liewald reaction time task: The Deary-Liewald task is the new, computer-based reaction time task. Simple Reaction Time (SRT) and Choice Reaction Time (CRT) were estimated using this task. In the SRT, participants were requested to press a button or key in response to a single stimulus. In the CRT, there would be four stimuli and participants would have to press the button that corresponds to the correct response. SRT involved eight practice trials and twenty test trials and CRT involved eight practice trials and forty test trials. For SRT, the stimulus to respond was the appearance of a diagonal cross within the square. Each time a cross appeared, participants would have to respond by pressing a key as quickly as possible.⁵ The results were computed and analyzed.

For the CRT, four white squares would be positioned in a horizontal line across approximately the middle of the computer screen, set against a blue background. Four keys on a standard computer keyboard corresponded to the different squares. The z key corresponds to the square on the far left; the x key to the square second from the left; the comma key to the square second from the right and the full-stop key to the square on the far right. The stimulus to respond would be the appearance of a diagonal cross within one of the squares. A cross would appear randomly in one of the squares and participants were asked to respond as quickly as possible by pressing the corresponding key on the keyboard. Each cross would remain on the screen until one of the four keys to be pressed, after which it would disappear and another cross appeared shortly after. The computer programme calculated the mean, median, variance, and standard deviation of the response times of the participants.

Procurement of Permissions: The protocol and the benefits of this study were explained to the subjects and written consent was obtained from all participants.

Ethical Consideration: This study was presented before Institutional ethics committee and IEC certificate was obtained.

Confidentiality: Confidentiality was maintained for the results generated from this study.

Analysis of Data: Statistical analysis was performed using Graph Pad Prism software (Graph Pad, San Diego, CA, USA) by unpaired t test.

OBSERVATIONS AND RESULTS: The study was conducted among 50 Diabetics and 50 age and sex matched controls. Baseline characteristics of the subjects were compared in Table-1.

Characteristics	Group-1 (n=50) Mean $\pm$ SD	Group-2 (n=50) Mean $\pm$ SD	p value
Age	56.4 $\pm$ 8.85	58.22 $\pm$ 8.20	0.2902
Fasting blood sugar (mg/dl)	98.02 $\pm$ 18.97	71.18 $\pm$ 5.07	0.0001*
Post prandial blood sugar (mg/dl)	146.35 $\pm$ 36.04	108.98 $\pm$ 5.81	0.0001*

Table 1: Baseline data of the subjects: -Group-1 (Diabetics) and Group-2 (Non Diabetics)

The mean age of diabetic was 56.4 with standard Deviation (SD) of 8.85 and non-diabetic was 58.22 with 8.20 SD and the difference between two group were not significant. However the diabetic group exhibited significantly higher fasting and post prandial blood sugar ($p < 0.05$).*(Table 1).

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Test	Group-1 Mean $\pm$ SD	Group-2 Mean $\pm$ SD	p value
ACE III Score	81.00 $\pm$ 8.10	83.92 $\pm$ 4.37	0.0272*

Table 2: Comparison of ACE-III scores between Group-1 and Group-2

The ACEIII score varied between diabetic and non-diabetic .The difference between the two group were statistically significant [$p < 0.05$]*. [Table 2].

Test	Group-1 Mean $\pm$ SD	Group-2 Mean $\pm$ SD	p value
SRT [ms]	359.76 $\pm$ 90.92	308.73 $\pm$ 63.38	0.0017*

Table 3: Comparison of Simple Reaction Time [SRT] between Group-1 and Group-2

When SRT was conducted between two groups, it was found out that the Diabetic group took longer time than Non Diabetic group and the difference was found statistically significant. [$P < 0.05$.]* [Table 3].

Test	Group-1 Mean $\pm$ SD	Group-2 Mean $\pm$ SD	p value
Choice ReactionTime[CRT][ms]	505 $\pm$ 106.58	461 $\pm$ 49.85	0.0093*

Table 4: Comparison of Choice Reaction Time [CRT] between Group-1and Group-2

The study of CRT showed significant [$p < 0.05$] variation between the two groups. The non-diabetic took lesser time than diabetic group (Table 4).

DISCUSSION: Our study clearly shows that type 2 diabetics are at increased risk of developing dementia. It is also clear that information processing is slower in type 2 diabetics compared to age and sex matched controls. Studies concerned with cognitive decline in type 2 diabetics are very rare. One such study.⁶ shows that the diabetics showed decreased Mini Mental Status Examination Scores (MMSE).

This present study utilized Addenbrooke's Cognitive Examination (ACE-III) scores for detecting dementia. The most widely used and validated test is The Mini-Mental State Examination (MMSE) but it has certain limitations such as insensitivity to detect early stages of impairment and the use of simple tasks for language and memory functions. A Meta-analysis done recently showed overall accuracy in detecting dementia favored Addenbrooke's Cognitive Examination scores when compared to MMSE scores.⁷

Cognitive changes are the known long-term complication in type 2 diabetes mellitus. Diabetes might accelerate the cognitive decline, which can be explained by many possible mechanisms like the disturbance in insulin and glucose homeostasis in the brain. Insulin resistance

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and advanced products of glycosylation do play a definitive role in cognitive decline in diabetics.⁸ Glial cells particularly astrocytes function is deranged in patients with diabetes, which also could explain the cognitive decline in diabetics.⁹

The finding of this study revealed that the simple and choice reaction time was found to be delayed in the diabetes mellitus group. Possible mechanisms for this derangement include the axonal degeneration of both myelinated and unmyelinated fibres, axon shrinkage, axonal fragmentation, thickening of basement membrane and micro thrombi ultimately leading to delayed motor nerve conduction velocity in diabetes.^{10, 11,12}

Implications: One of the greatest risk a diabetic with cognitive lapse may face is that, he/she may pop a wrong tablet or may not be aware whether he/she has taken it or not and may consume a hypoglycemic agent too many times which ultimately may lead the patient to a devastating hypoglycemia. Deterioration of the fluidic intelligence (the decision making skill) may prove fatal in drivers with diabetes. It is essential to educate the diabetic patient and more importantly their kins about the cognitive deficit and alarm them of the consequences cognitive laps.

CONCLUSION: Patients with type 2 diabetes are at increased risk of developing cognitive decline and delayed information processing when compared to non-diabetics. The routine assessment of the diabetic complications should include the evaluation of the dementia preferably using Addenbrooke's Cognitive Examination (ACE-III) scores and information processing should also be assessed using simple and choice reaction times by the dialectologists while their patients visiting them for follow up.

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