Assessment of Cognitive Status in Type 2 Diabetes

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Abstract

Introduction: The increasing prevalence of diabetes over the world has become an important public health problem. Diabetes is considered a non-communicable disease nowadays, with about 173 million diabetic people over the world. Generally, problems for the elderly are impaired activities of daily living (ADL) and cognitive dysfunction. Central nervous system involvement is increasingly recognized as a possible complication of diabetes. Cognitive impairment might be another factor associated with poor diabetes control and also with bad adherence of patients to educational approaches, such as diet orientations.

Objective: To assess the cognitive impairment in type 2 diabetes.

Methods: A cross sectional study was designed and patients were recruited from Abbasi Shaheed Hospital with a non-probability convenient sampling. Patients having type 2 diabetes over 30 years of age were included and patients with blindness, stroke and psychiatric disorders were excluded. Sample size was done by using the WHO software and a sample of 200 cases was collected. Mini Mental State Examination (MMSE) scale was the data collection tool. Cronbach's a coefficient of 0.54 – 0.96. Sensitivity & Specificity reported an average *sensitivity* of 75% among dementia patients and reported *specificity* of 62% - 100%. The study protocol was approved by ethical review committee.

Results: A one-way multivariate analysis of variance was run to determine the effect of diabetes on cognitive impairment among the four clinical parameters of cognition. The difference in cognitive impairment between the four clinical parameters of cognition was statistically significant.

Conclusion: The diabetes associated with HCV is more as compared to HBV.

Key words: Diabetes & Cognition, HBV, Type 2 Diabetes

Introduction

The increasing prevalence of diabetes over the world has become an important public health problem. Diabetes is considered a non-communicable disease nowadays, with about 173 million diabetic people over the world. As population is increasing, getting older, more obese and sedentary, the number of individuals with diabetes also increase.[1] Although prevention of diabetes is being promoted worldwide, patients with diabetes or glucose intolerance continue to increase. Coupled with the aging of society, an increase in the number of elderly diabetic patients is therefore inevitable. Generally, problems for the elderly are impaired activities of daily living (ADL) and cognitive dysfunction. Central nervous system involvement is increasingly recognized as a possible complication of diabetes.[2] Diabetes increases the economic burden on poverty stricken societies in Pakistan, which only intensifies their already unhealthy and risky life styles.[2]

Pakistan stands on number 6 among the Top Ten countries having increased burden of diabetes mellitus.[3] According to the International Diabetes Federation (IDF), Pakistan had 6.2 million people with diabetes in 2003. By 2025 the number of people affected by diabetes is expected to rise to well over 14.5 million. Six million people are currently suffering from impaired glucose tolerance, and will eventually contract diabetes. Although diabetes is considered to be risk factor for cognitive impairment the cognitive function of patients with type 2 diabetes is not usually evaluated in routine clinical care.[4]

Many mechanisms have been considered for an association between diabetes and cognitive dysfunction. In their review, Biessels et al mentioned that: (i) atherosclerosis, such as brain infarcts; (ii) microvascular disease as a result of insidious ischemia; (iii) advanced protein glycation and oxidative stress as a result of glucose toxicity.[4]

Recently, interesting findings have been reported for longitudinal research. The Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications

(DCCT/EDIC) study, a long-term study that followed up type 1 diabetes patients for approximately 18 years, found that a decline in cognitive function, such as motor speed and psychomotor efficiency, was associated with glycemic control level.[5,6] In contrast, the Action to Control Cardiovascular Risk in Diabetes-Memory in Diabetes (ACCORD-MIND) trial, whose aim was intensive control in type 2 diabetes patients, observed a decline in cognitive function over time, and effects of intensive glycemic control were not shown.[7,8]

Cognitive impairment might be another factor associated with poor diabetes control and also with bad adherence of patients to educational approaches, such as diet orientations. The diabetic community lacks the facilities for screening and monitoring and the drugs which can ensure a healthy, 'normal,' life for people with diabetes. Low literacy rates in Pakistan suggest that if diabetes awareness campaigns are to be successful, media must be involved. Education programs on health issues, promoting a healthy lifestyle, and focusing on sound dietary habits and exercise are needed. Warnings about the hazards of diabetic complications should also be emphasized.

Insufficient data is available regarding frequency of cognitive impairment in diabetes in Karachi, Pakistan. The aim of our study is to evaluate the cognitive status of patients with type 2 diabetes.

Materials and Methods

Study design: Cross sectional study

Place and duration of study: Patients attending OPD of Abbasi Shaheed hospital from June 2013 till June 2014.

Sampling technique: Non probability convenient sampling.

Inclusion criteria:

1. Patients having type 2 diabetes when diabetes was diagnosed after 30 years of age.

Exclusion Criteria:

1. Blindness, illiterate, stroke, and psychiatric disorders.
2. Patients not willing to participate in the study.

Sample size:

Sample size calculation is done by using WHO software: Level of significance (alpha) = 0.5 (margin of error), Power of the test (1-β) = 95, Anticipated population proportion P1 = 0.43, Anticipated population proportion P2 = 0.16, Sample size n = 60. A sample of 200 cases and controls were collected to avoid the chances of type II error.

Data Collection:

Cognitive impairment in type -2 Diabetes data from a total of 200 patients (diagnosed after 30 years of age) was collected and data was stratified according to age, gender and socioeconomic status. The tool use for data collection was a questionnaire called as Mini Mental State Examination (MMSE) scale.[9,10,11] It is a brief screening tool to provide a quantitative assessment of cognitive impairment and to record cognitive changes over time. Patients were explained regarding the purpose of study and an informed consent was taken. Data collection tool was by Questionnaire method by MBBS students. Uniform administration of questionnaire in URDU, (standard language e.g. urdu) was conducted.

Reliability of MMS:

Tombaugh & McIntyre reported moderate to high test-retest reliability citing correlations of 0.38 to 0.99 in studies having a retest interval of < 2 months (24/30 studies r >0.75). Inter-observer reliability: Concordance correlation coefficient = 0.87 between evaluations performed by GPs & those performed by psychologists. Internal consistency: Cronbach's a coefficient of 0.54 – 0.96 reported by Tombaugh & McIntyre.[12]

Validity of MMS:

Concurrent Validity: Tombaugh & McIntyre (1992) reported correlations of 0.70 to 0.90 between MMSE scores and other measures of cognitive impairment. Sensitivity & Specificity: reported an average *sensitivity* of 75% among dementia patients and reported *specificity* of 62% - 100%.[12,13]

The Mini-Mental State Exam:

Evelyn Lee Teng, Ph.D., and Helena Chang Chui Department of Neurology University of Southern California Keck School of Medicine, was used to assess the four clinical parameters of cognition. Orientation (maximum score=10), Registration (maximum score=3), Attention and Calculation (maximum score=5), Recall (maximum score=3), Language (maximum score=9).[9]

Administration and Scoring of the Individual Items

PLACE AND DATE OF BIRTH**:** This item is a measure of long-term memory.

First ask "WHERE WERE YOU BORN?", then ask "WHEN WERE YOU BORN?"

Scoring: One point for each entry. Tell the subject: "I AM GOING TO SAY THREE WORDS FOR YOU TO REMEMBER. REPEAT THEM AFTER I HAVE SAID ALL THREE."

Say the three words at the rate of l.5 sec per word. MENTAL REVERSAL**:** This item has two parts: counting backwards from 5 to l, and spelling WORLD backwards. Score 2, 1, or 0 for

counting according to the stated criteria on the record form .Score from 0 to 5,for spelling. TEMPORAL ORIENTATION**:** Year ,scoring from 8-0 , DATE (of the month, scoring from 3-0,DAY (of the week) scoring 1-0.Ask "WHAT IS TODAY's DATE?" SPATIAL ORIENTATION: State, County ,City .Store/Hospital(Clinic)/ Home? Ask "WHAT ___ ARE WE IN?" NAMING**:** Asks "WHAT IS THIS?", and then points to a watch for the 3MS Test sub-items, the examiner asks while pointing to the appropriate part on his or her own body:

"WHAT DO YOU CALL THIS PART OF THE BODY? Score 1 point for each item named correctly within 2sec. FOUR-LEGGED ANIMALS (30 sec) discontinue after 30 sec. or after 10 correct responses. SIMILARITIES**:** ARM-LEG : Scoring 2-0 LAUGHING-CRYING:2-0 EATING-SLEEPING :2-0. Introduce saying:"AN APPLE AND A BANANA ARE ALIKE IN THAT THEY ARE BOTH FRUIT**."** Emphasize the words "alike" and "both.

REPETITION: Ask to repeat a sentence, HE WOULD LIKE TO GO HOME. "NO IFS ___ ANDS ___ OR BUTS ___".The intended function of this item is to assess attention and the ability to repeat orally presented verbal messages. Scoring:2 points for perfect repetition.1 point if there is 1 or 2 missed or wrong words .READ AND OBEY "CLOSE YOUR EYES." closing without promoting or after promoting. WRITING : Tell the subject:"I WOULD LIKE TO HAVE A SAMPLE OF YOUR HANDWRITING.WRITE 'HE WOULD LIKE TO GO HOME.'"Allow either cursive or printing. Allow up to one minute for response, then move on to the next item.

Scoring: One point for each word, but do not score the first word "I/He". Score each word according to whether or not it can be readily identified without the context. For each word, score 0 if there is spelling error or incorrect mixed capitalization .COPYING INTERSECTING PENTAGONS (l minute): Each Pentagon: 5 approx. equal sides 4 4,5 but un-equal (>2:1) sides 3 3,Other enclosed figure 2 2,2 or more lines 1 1,Less than 2 lines 0 0.Intersection:4-cornered enclosure 2,Not 4-cornered enclosure 1,No enclosure 0.Show only the lower one third of the sheet that contains the sample pentagons. For right-handed subjects,present the sample on their left side. For left-handed subjects, present the sample on their right side. This way the sample will not be blocked by the drawing hand. Allow up to one minute for response. Do mark the l min. point on the product during scoring, THREE-STAGE COMMAND: TAKE THIS PAPER WITH YOUR L (R) HAND,FOLD IT IN HALF, AND HAND IT BACK TO ME. This item tests the subject's ability in understanding, remembering, and executing a three-part command. The three parts of the command are spoken clearly in approximately 6 sec., without interruption, and are given only once. If the subject interrupts with "What did you say?" or the like, do NOT stop to respond; continue to finish the command, then say: "Do what you think I asked you to do."Use a blank piece of paper for this test. The first stage of the command asks the subject to take the pieces of paper with his or her NON-preferred hand (the hand not used in the preceding writing and drawing tasks). After saying the command, the examiner should take care not to move the paper towards the subject before he or she reaches for it; this is to avoid providing non-verbal cues for the subject to take the paper. Do not repeat any part of the command. If the subject requests the examiner to do so, say "SORRY, I CANNOT REPEAT. JUST DO WHAT YOU THINK I ASKED YOU TO DO." If the circumstances are such that it is desirable to oblige for the sake of maintaining a fragile rapport, score according to the response(s) executed before the repeat presentation of the command. Scoring One point for each part of the command. First part: Score 0 if the subject uses the preferred hand. Second part: Score 0 if the subject folds the paper more than once. Third part:

Score 0 if the subject simply puts the paper down instead of handing it back to the examiner. The subject may fold the paper with both hands, and may hand back the paper with either hand. SECOND RECALL OF THREE WORDS: (Clothing: SHOES/SHIRT/SOCKS) 0 1 2 3 (Color: BLUE/BLACK/BROWN) 0 1 2 3 (Virtue: HONESTY/CHARITY/MODESTY) 0 1 2 3. Always administer this item, even if the subject has scored 0 on First Recall.[9]

Statistical Analysis

Descriptive Statistics of four clinical parameters of cognition (orientation score, registration score, attention calculation score, recall score, language score) were computed. Cognition was categorized into three categories of (cognitive impairment <23, borderline 23 and normal >23) and ANOVA was used to compute F and *p*-values. Post hoc test was used to verify the differences between cognitive impairment <23, borderline 23 and normal >23 among the four clinical parameters of cognition. (Table 1)

Results

A one-way multivariate analysis of variance was run to determine the effect of diabetes on cognitive impairment among the four clinical parameters of cognition. The orientation mean scores were 7.07±2.97 which were near normal as compared to normal orientation score of 10.

The registration mean scores were 3.0±0.00 which were also normal as compared to normal registration score of 3.

The attention calculation mean scores were 2.57±1.98 which were low as compared to normal attention calculation score of 5, indicating cognitive impairment.

The recall mean scores were 1.78±0.97 which were also low as compared to normal recall score of 3, indicating cognitive impairment.

The language mean scores were 6.7±1.52 which were also low as compared to normal language score of 9, indicating cognitive impairment.

The difference in cognitive impairment between the four clinical parameters of cognition was statistically significant, $F(8,116) = 13.53$, $p<0.0001$; Wilks' $\Lambda = 0.017$; partial $\eta^2 = 0.871$. (Table 2)

Tukey Post Hoc test:

There was statistically significant difference among the categories of cognition (normal >23, borderline= 23, cognitive impairment <23) in orientation score and attention calculation score. (Table 3)

Discussion & Conclusion

Low cognition was observed in diabetics. Moreover majority of studies involved old age research participants, having type II diabetes representing reduced cerebral functions. Since the arrangements of cognitive weakening which is linked to normal senescence are quite comparable to the particular patterns stated in senior diabetic participants, the pathogenic mechanisms claim that as the age of an individual advances and the person is diabetic, so they might be behaving synergistically, which can implicate in the form of neurobehavioral damages. Considering this fact into regard, research participants who are more than 55 years of age, were employed in the research study, in order to curtail the influence of aging on the functions of their cerebrum. Among the group, age as a factor did not have a substantial implication on the psychometric tests performance. In current research, no noteworthy relationship existed between disease duration and abnormalities in cognitive function; contrasting the view that disease duration is an important predictor of major complications in terms of diabetes, for instance retinopathy and nephropathy.[14,15,16,17]

Moreover the functioning of cognition in patients having type II diabetic connected well with disease duration among few research participants in some studies but it was not a general trend seen in all research studies. There was no important relationship among the patient's performance in psychometric tests and their blood glucose levels. Even though, in total, patients having type II diabetes demonstrated inferior cognitive function test scores, and vice versa. Additionally, it can be assumed that on long term basis, diabetic patients can have cognitive damages, which might be linked to a state of comparative neuroglycopenia due to reduced glucose transfer through the barrier of blood-brain.[18,19,20]

In such a scenario, sophisticated levels of blood glucose can lead to enhancement in cognitive function measurements, on short term basis. All in the entire conclusion derived from psychometric tests show that patients having diabetes showed poor performance in tests of recent memory, repetition and attention, as compared to the control group. In previous researches conducted patients having type II diabetes, depicted distinct relationship among performance on tests and presence of peripheral neuropathy. To sum up, we propose that cognitive dysfunction must be known as a certain impediment of enduring type II diabetes. We endorse that there must be more awareness in health practitioners who are linked to care of diabetic patients.[21,22,23,24,25,26]

Recommendations

According to Diabetes Care longer period of diabetes may be linked with poorer scores, but hypoglycemic therapy may improve cognitive scores.[27]

As mentioned by Bayer pharmaceuticals[28]

- Take your insulin daily, as prescribed by your doctor. Do not stop taking your insulin when you are sick, unless your doctor tells you to. Your insulin dose may change when you're sick, injured, have an infection or are emotionally distressed. During these times, test your

blood glucose frequently and call your doctor or diabetes educator for needed insulin changes.

- Follow your doctor's instructions when changing insulin doses.
- Before opening an insulin bottle, check the expiry date. Once opened, an insulin bottle or cartridge is good for one month.
- Before taking insulin, check the vials for frosty rings around the neck, clumping of particles or insulin that won't mix. Do not use the insulin if it displays any of these characteristics.
- Do not change the brand of insulin you are using without asking your doctor.
- Keep the bottle of insulin you are using at room temperature, and a spare bottle in the fridge. Do not expose insulin to extreme heat or cold.
- Insulin injections are more comfortable when the insulin is at room temperature.
- If using a syringe and mixing short and intermediate acting insulins, the short-acting* insulin should be drawn up first.
- Rapid-acting insulin should be administered zero to 15 minutes before eating. Short-acting* insulin should be administered 30 to 45 minutes before eating.
- Rapid acting insulin should not be mixed in a syringe with intermediate or long acting insulin.
- Long acting insulin must not be mixed with any other insulin.
- Have a glucagon kit available in case you have severe low blood glucose and become unconscious. Glucagon, available by prescription only, is injected to make the liver release glucose to raise your blood glucose. Family members should know how to use it.

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Conflict of Interest: The authors declare that they have no competing interests.

Ethical Considerations

The study protocol was approved by ethical review committee. Written informed consent was taken from the participants before their enrolment in this study. The participants' involvement in this study was voluntary and no financial incentives were provided to any study participant.

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Table 1: Descriptive Statistics

Clinical Parameters	Mean ± SD
Orientation Score	
Cognitive Impairment <23	4.33 ± 2.06
Border line 23	8.0 ± 2.0
Normal >23	9.8 ± 0.44
Registration Score	
Cognitive Impairment <23	3.0 ± 0.00
Border line 23	3.0 ± 0.00
Normal >23	3.0 ± 0.00
Attention Calculation Score	
Cognitive Impairment <23	0.5 ± 0.54
Border line 23	3.66 ±1.15
Normal >23	4.40 ±0.54
Recall Score	
Cognitive Impairment <23	1.5 ± 1.22
Border line 23	1.6 ± 1.15
Normal >23	2.2 ± 0.44
Language Score	
Cognitive Impairment <23	5.83 ± 1.32
Border line 23	6.66 ± 0.57
Normal >23	8.00 ± 1.41

Table 2: ANOVA

Clinical parameters	**F**	***p*-value**
Orientation Score	15.47	0.001
Registration Score	--	--
Attention Calculation Score	47.20	0.0001
Recall Score	0.69	0.51
Language Score	4.04	0.048

Cognition: Multivariate Tests					
Wilks' Lambda Value	F	Hypothesis df	Error df	Sig.	Partial Eta Squared (η^2)
0.017	13.53	8.00	16.00	0.0001	0.871

Table 3: Post Hoc test

Clinical Parameter	Cognition		*p*-value
Orientation score	Cognitive impairment <23	Borderline 23	.024
		Normal >23	.001
	Borderline 23	Cognitive impairment <23	.024
		Normal >23	.333
	Normal >23	Cognitive impairment <23	.001
		Borderline 23	.333
Attention calculation score	Cognitive impairment <23	Borderline 23	.000
		Normal >23	.000
	Borderline 23	Cognitive impairment <23	.000
		Normal >23	.356
	Normal >23	Cognitive impairment <23	.000
		Borderline 23	.356
Recall score	Cognitive impairment <23	Borderline 23	.970
		Normal >23	.501
	Borderline 23	Cognitive impairment <23	.970
		Normal >23	.751
	Normal >23	Cognitive impairment <23	.501
		Borderline 23	.751
Language score	Cognitive impairment <23	Borderline 23	.631
		Normal >23	.040
	Borderline 23	Cognitive impairment <23	.631
		Normal >23	.352
	Normal >23	Cognitive impairment <23	.040
		Borderline 23	.352