

A study to evaluate the relationship between diabetes mellitus and cognitive dysfunction



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ABSTRACT

Background: Diabetes mellitus (DM) is the most common endocrine disorder. It leads to slow progressive end-organ damage (both microvascular and macrovascular). The cognitive dysfunction is a less known and less addressed complication of DM. **Aims and Objectives:** This study aims to evaluate the cognitive dysfunction in the patient with DM and to assess the cognitive dysfunction by Mini-Mental State Examination (MMSE) of the patients who are suffering from DM. **Materials and Methods:** A total of 979 diabetic patients were screened for cognitive dysfunction using MMSE score. The patients were evaluated as per the history. MMSE is a 30-point questionnaire which is mainly used to measure the cognitive impairment. **Results:** A total of 979 diabetic patients were included in the study out of which 44.7% of the patients were found to have cognitive dysfunction. Cognitive impairment was more prevalent in female diabetics (51%) as compared to male diabetics (39.8%). The result is significant at $P < 0.05$. Patients with longer duration of diabetes had much higher incidence of cognitive impairment (80.9%) as compare with the patients with short duration of diabetes which has lesser incidence of cognitive impairment (16.2%). $P < 0.001$ was considered statistically significant. **Conclusion:** Majority of the subjects suffering from DM have concomitant cognitive impairment. There is a significant cognitive impairment seen in subjects with DM. Early recognition and management of the cognitive dysfunction will help in improving quality of life.

Key words: Cognitive impairment; Diabetes; Screening by Mini-Mental State Examination score

INTRODUCTION

Diabetes mellitus (DM) is the most common endocrine disorder. It leads to slow progressive end-organ damage in multiple sites. Constant hyperglycemia is a significant cause for the development of micro- and macrovascular complications of DM such as renal, cardiac, neurological, and retinal which are well known and widely accepted.¹ However, cognitive dysfunction is a less addressed complication of DM. The management of DM includes self-management behaviors with highly involved parameters such as blood sugar monitoring, diet charting, and medications. Diabetic subjects with cognitive impairment have difficulty in managing their problem. The Mini-Mental State Examination (MMSE) is a questionnaire which tests several aspects of cognitive domains – “orientation,

registration, verbal recall, calculation, visual construction, attention, and language.”² MMSE score can be used for the assessment of cognitive impairment in diabetic patients.

Aims and objectives

The aim of this study is to evaluate the cognitive dysfunction in the patients with DM using MMSE.

MATERIALS AND METHODS

This was an observational cross-sectional study done from January 2020 to June 2021 in Sanjay Gandhi Memorial Hospital, associated with Shyam Shah Medical College, Rewa (M.P.) Informed consent was obtained from all the study subjects (S. No/IEC/SS/MC/2020/4271 REWA

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Date February 20, 2020). Patients with prior diagnosis of diabetic mellitus were evaluated with history and clinical examination including MMSE score.

The following are the MMSE Grading³ scores: - Normal – 24–30, Grade-I 19–23 (mild), Grade-II 10–18 (moderate), and Grade-III ≤9 (severe).

Sample size

A total of 979 patients of DM admitted to Shyam Shah Medical College and Sanjay Gandhi Memorial Hospital were included in the study.

Inclusion criteria

The following criteria were included in the study:

- >18 years of age group
- Patient consenting for study
- Patient diagnosed with DM.

Exclusion criteria

- Epilepsy and anti-epileptic drug, hypothyroidism, Alzheimer disease, Parkinson disease, >60 years of age, malignant hypertension, alcohol abuse, critical ill patient, electrolyte imbalance, pregnancy, stroke, and patient not consenting for study were excluded from the study.

Data collection and methods

Patients included in the study underwent history taking followed by clinical examination and relevant investigations. MMSE score was calculated for each patient. Data thus obtained were recorded in a predesigned questionnaire.

Statistical analysis

Data were entered into Microsoft Excel worksheet. Observation tables prepared using the data were analyzed by

GraphPad software. Chi-square test was used for calculating P-values. P<0.01 was considered statistically significant.

RESULTS

The study's 979 patients included, the largest proportion of cognition dysfunction (86.65%) was found in older age group (51–60) while the smallest proportion (2.27%) was found in younger age group (18–30). The Chi-square statistic is 524.813. P<0.001 was considered statistically significant. The result is significant at P<0.05 (Table 1).

Out of 979 patients included in the study, 39.85% of males had cognitive dysfunction while 51.05% of females had cognitive dysfunction. Overall 44.73% of patients had cognitive dysfunction. The Chi-square statistic is 12.3175. P=0.0021 was considered statistically significant. The result is significant at P<0.05 (Table 2).

The study's 979 patients included, Diabetics of less than 5 years duration had mostly normal MMSE, while those with more than 5 years of disease had mostly Grade I impairment of MMSE, among the 979 patients included in the study, 548 patients had duration <5 years. 459(83.75%) patients amongst them, were found to be normal whereas 89(16.25%) patients were found to have cognitive dysfunction and 431 patients had duration more than 5 years. 82(19.03%) patients amongst them, were found to be normal whereas 349(80.97%) patients were found to have cognitive dysfunction. The Chi-square statistic is 409.6302. P<0.001 was considered statistically significant. The result is significant at P<0.05 (Table 3).

The study's 979 patients included, Majority of patients (55.26%) had normal cognition. Out of cases, 43.61%

Table 1: Age-wise comparison of MMSE grade in patients

Age groups	No. of cases	MMSE GRADE				% of cases with cog. dysfunction
		Normal	Grade-I	Grade-II	Grade-III	
18–30	44	43	1	0	0	2.27
31–40	133	126	7	0	0	5.26
41–50	375	307	65	3	0	18.13
51–60	427	57	362	8	0	86.65
Total	979	534	434	11	0	NA

MMSE: Mini-Mental State Examination

Table 2: Gender-wise comparison of MMSE grade in patients

Gender	No. of cases	MMSE Grade				% of cases with cognitive dysfunction
		Normal	Grade-I	Grade-II	Grade-III	
Male	552	332	215	5	0	39.85
Female	427	209	212	6	0	51.05
Total	979	541	427	11	0	NA

MMSE: Mini-Mental State Examination

Table 3: Comparison of duration of diabetes with MMSE grade

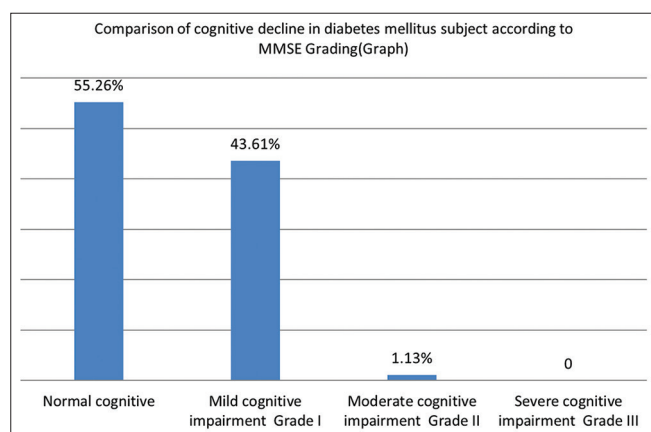
Duration of DM	No. of cases	MMSE score				% of cases with cognitive dysfunction
		Normal	Grade-I	Grade-II	Grade-III	
<5 years	548	459	89	0	-	16.24
>5 years	431	82	338	11	-	80.97
Total	979	541	427	11	-	-

MMSE: Mini-Mental State Examination

Table 4: Grades of cognitive impairment in patients

MMSE grades	No. of dm cases	Percentage
Normal cognition	541	55.26
Mild cognitive impairment Grade I	427	43.61
Moderate cognitive impairment Grade II	11	1.13
Severe cognitive impairment Grade III	-	-
Total	979	100.00

MMSE: Mini-Mental State Examination, DM: Diabetes mellitus

**Figure 1: Grades of cognitive impairment in patients**

had mild cognitive impairment while only 1.13% cases had moderate cognitive impairment. None of the cases had severe cognitive impairment (Table 4 and Figure 1).

DISCUSSION

In the present study, 979 diabetic patients were taken as the study group and cognitive impairment was studied with respect to age, sex, duration of diabetes, and glycemic control. The cognitive status of patients was evaluated through MMSE. In this study, 43.61% of patients had mild cognitive impairment whereas 1.13% of patients had moderate cognitive impairment. About 55.26% of patients had normal cognition. There was a significant decrease in MMSE score among the diabetics ($P < 0.05$). The mean MMSE score was 23.84 ± 1.73 .

Shuba assessed the cognitive status of type 2 diabetics through MMSE and compared the mean MMSE scores with non-diabetics. They found that type 2 DM is related to cognitive dysfunction.⁴ Another study done by Seyfardini, strongly supported the relation of type 2 DM and cognitive dysfunction.⁵ Kalar et al., also observed the same.⁶ Tekin et al., described that type 2 diabetes destroys cognitive function.⁷

Dey et al., in his study, found that cognitive dysfunction should be considered as a possible long-term definite complication of type 2 diabetes.⁸ Kataria et al., identified high frequency of cognitive decline in several domains of cognitive function in type 2 DM subjects. Mukherjee et al., also described that impairment in cognition is related with type 2 DM.⁹

Long-term hyperglycemia increases the chance of cerebral microvascular as well as macrovascular complication, and these complications lead to cognitive abnormalities. Hence, it is considered as a contributing factor for neurological changes (structural and functional) in diabetics.

Hyperglycemia gives increased substrate for lactate formation which worsens the acidosis within cells and the glutamate accumulation causes extensive neuronal damage.¹⁰ Damage to neurons and vascular endothelium also occurs due to the high osmotic stress caused by hyperglycemia which, in turn, disrupts the blood-brain barrier leading to the leakage of vascular substances which further enhances neuronal damage.¹¹

Cognitive dysfunction and age

In our study, only 2.27% of cases in 18–30 age group, 5.26% of cases in 31–40 age group, 18.13% of cases in 51–60 age group, and 86.65% of cases in 51–60 age group had cognitive dysfunction, showing a sharp increase in cognitive dysfunction at older age in diabetic patients. Most of the studies suggest that cognitive impairment is more prevalent in older patients, as compare to young patients.

Tiwari et al., in their study, reported that type 2 DM is a risk factor for impairment in cognitive functions irrespective of the cutoff age of either 60 years or 55 years.¹² Ding et al., explained that cerebral microvascular disease may

accelerate the age-linked decline of cognitive functions observed in diabetic people.¹³

Cognitive dysfunction and gender

In our study, 39.85% of males had cognitive dysfunction while 51.05% of females had cognitive dysfunction. The difference was statistically significant. Therefore, female diabetics are more likely to have cognitive dysfunction compared to males. Kim *et al.*, (2017),¹⁴ in a large Korean cohort, found that T2DM was an independent risk factor for dementia only in women.

In a study conducted by Yu *et al.*, (1989), prevalence and predictors of neurocognitive impairment in T2DM, one study reported the risk of cognitive impairment even higher (3.75 times) in women.¹⁵

Cognitive dysfunction and duration of diabetes

The study's 979 patients included, Diabetics of <5 years duration had mostly normal MMSE, while those with more than 5 years of disease had mostly Grade I impairment of MMSE, among the 979 patients included in the study, 548 patients had duration <5 years. 459(83.75%) patients amongst them, were found to be normal where as 89(16.25%) patients were found to have cognitive dysfunction and 431 patients had duration more than 5 years. 82(19.03%) patients amongst them, were found to be normal whereas 349(80.97%) patients were found to have cognitive dysfunction.

As per studies conducted by Wessels *et al.*, (2008), and Reijmer *et al.*, (2010), chronic hyperglycemia and long duration of diabetes are both associated with increased development of cognitive dysfunction.^{16,17}

Limitations of the study

1. Given the cross-sectional design, self-reported duration of diabetes is not reliable because it only provides information on the time of diagnosis of diabetes, not when these disease processes first began
2. A cohort study with larger sample size will help to examine the change in cognitive function in association with diabetes
3. MMSE is considered as a screening test. Furthermore, the subjects were examined only once, thus numerous assessments are needed for accurate confirmation of decrements.

CONCLUSION

DM is a common endocrine disorder which leads to micro- and macrovascular complications. Cognitive dysfunction is a less addressed complication of DM. Compelling evidence suggest that people with DM are at

increased risk of developing cognitive impairment. Early recognition and management of the cognitive dysfunction will help in improving quality of life and it promotes independent living in diabetic patients.

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Authors' Contributions:

RKP- Concept and design of the study, prepared first draft of manuscript; **KSK**- Interpreted the results; reviewed the literature; and manuscript preparation; and **SE**- Concept, coordination, statistical analysis and interpretation, preparation of manuscript, and revision of the manuscript.

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