

## Research Article

# Study of mild cognitive impairment by applying Kolkata cognitive screening battery in type 2 diabetes mellitus patients in India

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## ABSTRACT

**Background:** Several prospective, large, population-based cohort studies have found that diabetes is associated with an increased risk of mild cognitive impairment (MCI). This study was aimed to determine the relationship between diabetes mellitus (DM) and MCI with respect to age of onset, duration, other co-morbidities, complications of diabetes and the effect of HbA1c on MCI, using Kolkata cognitive screening battery.

**Methods:** From 1<sup>st</sup> December 2014 to 31<sup>st</sup> May 2015 a unicentric, case control study was designed to include patients attending the medicine outpatient clinic of LTMGH as per the inclusion and exclusion criteria. The cognition was assessed by Kolkata cognitive screening battery and the scores were compared with control subjects to rule out cognitive decline. A score below 110 was taken as the cut-off for identifying the significantly impaired.

**Results:** 50 patients were included in study (mean age 57.02 years). The mean MCI score was 100.58 in the diabetic group, which was significantly less as compared to 123.35 as seen in the control group. Object naming test was the least affected. Furthermore, MCI had positive significant correlation ( $p < 0.05$ ) with nephropathy ( $p < 0.05$ ), retinopathy ( $p < 0.05$ ), HbA1c ( $p < 0.05$ ) and duration of DM ( $p < 0.05$ ). There was no significant co-relation between the sex of the patients and MCI ( $p > 0.05$ ).

**Conclusions:** There is a strong correlation of MCI with HbA1c. This implies that control of diabetes may help improve cognition and help in better management of diabetes as MCI disrupts the individual's lifestyle and interferes with day-to-day activities. The results of our study warrant future research to improve our understanding regarding MCI and its correlation with diabetes.

**Keywords:** Aging, Cognitive function, Diabetes, Dementia, Risk factors

## INTRODUCTION

Mild cognitive impairment (MCI) also called early dementia is an intermediate stage between the expected cognitive decline due to normal aging and impaired cognition as observed in dementia. A person who has MCI is able to carry out daily activities without difficulty but a particular subset of cognitive skills may be diminished, whereas in a person suffering from dementia, memory loss is severe enough to interfere with someone's ability to function socially at work. The

concept of MCI emphasized memory impairment and its status as a precursor state for Alzheimer disease (AD). Gender, race, and lower education are inconsistently associated with MCI in various studies. Subsequently, it was recognized that MCI can be heterogeneous in terms of clinical presentation, etiology, prognosis, and prevalence. Elevated blood pressure, mid-life diabetes, obesity, cardiac disease, and apo-lipoprotein E epsilon 4 genotype have also been associated with increased risk of MCI or certain subtypes of MCI, and alcohol use has been associated with decreased risk. Several prospective,

large, population-based cohort studies have found that diabetes is associated with an increased risk of cognitive decline and dementia.<sup>1</sup>

A systematic review of 14 studies found that diabetes is associated with a 50 to 100 percent increase in risk of Alzheimer's disease (AD) and of dementia over all, and a 100 to 150 percent increased risk of vascular dementia.<sup>2</sup> In patients having uncontrolled blood sugar, precisely >7%, deficits have been seen in the areas of psychomotor efficiency, problem solving, planning, functions mediated by frontal lobe like executive functions, insight, reasoning.<sup>3</sup>

Aim of this study was to determine the relationship between diabetes and MCI with respect to age of onset, duration, other co-morbidities, complications of diabetes and the effect of HbA1c on MCI.

In the study, diabetic patients were examined for the evidence of MCI using Kolkata cognitive screening battery. Very few studies have been conducted in our country to establish the correlation between MCI and Diabetes. If medical assistance is provided early, it will help to considerably reduce the co-morbidity rates. Thus, we attempted to conduct this study.

## METHODS

This was a unicentric, retrospective, case control study that aimed to: to study the incidence of MCI in diabetics, correlate MCI with duration of diabetes, age, sex and education, to compare MCI with HbA1c, blood sugar, nephropathy, retinopathy, comorbidities like hypertension, ischemic heart disease and asthma, to find out which particular cognitive function is impaired in MCI patients with respect to age, duration of diabetes, comorbidities and HbA1c. The following inclusion and exclusion criteria were used while enrolling the patients.

### Inclusion criteria

- Type II diabetics
- Patients ages 40 years and above of either sex
- Hindi, English, Marathi speaking subjects
- Ability to communicate and follow up the instructions given by the investigator

### Exclusion criteria

- Dementia according to DSM IV criteria
- History of significant hearing and visual impairment
- Family history of dementing illness
- History of neurological disorders (stroke, Parkinson's disease, active epilepsy) or psychiatrics (schizophrenia, mental retardation, illness, depression and mania) and substance abuse
- History of memory impairment observed by family members not matched with DSM IV criteria

- Hypothyroidism and vitamin B<sub>12</sub> deficiency
- Individuals living alone as the history and complaints cannot be corroborated with family members

### Study setting

Mumbai is the most populous city in India, with an estimated metropolitan area population of 20.7 million according 2011 census.<sup>4</sup> Greater Mumbai has a literacy rate of 94.7%, which is higher than the national average of 86.7%. Apart from Marathi, which is the native language, Hindi, Gujarati and English are spoken and understood well in this region. LTMGH, a 1400 plus bedded academic tertiary level hospital, is a major healthcare provider in Sion, Mumbai.

### Data collection and analysis

After approval from the ethics committee, diabetic patients having type 2 DM as per American Diabetic Association 2009 criteria, attending the medicine outpatient clinic of LTMGH were selected as per the inclusion and exclusion criteria. They were subjected to a structured interview, which included demographic information such as age, sex, literacy level and occupation. The cognition was assessed by Kolkata Cognitive Screening Battery.<sup>5</sup> It consists of:

- Category based verbal fluency tests
- A 15 item version of object naming test
- Mental state examination
- Calculation tests
- Word list memory task
- Visuo-constructional ability
- Delayed recall
- Delayed recognition word task

Information was corroborated with at least one close family member, usually the spouse, children or a reliable informant closely related with the test subject. The scores were compared with control subjects to rule out cognitive decline due to aging. A score below 110 was taken as the cut-off for identifying the significantly impaired. The data was collected during the period from 1<sup>st</sup> December 2014 to 31<sup>st</sup> May 2015. All the raw data was entered in Microsoft excel sheets and analyzed in SPSS statistical software (SPSS Inc, Chicago, USA).

## RESULTS

50 patients were included in study population with age of cases ranging from 40 to 80 years with average age being 57.02 years as compared to the control with an average age of 52.25 years. Among the 50 patients, 32% (n=16) belonged to the age group 40-50 years, 32% (n=16) to the age group 51-60 and 36% (n=18) to the age group >60 years (Table 1).

**Table 1: Characteristics of patient population.**

Age structure	
<b>Diabetic patients</b>	<b>n= 50 (mean age 57.02 years)</b>
40 to 50 years	16
51-60 years	16
More than 60 years	18
<b>Control patients</b>	<b>n= 20 (mean age 52.25 years)</b>
Mean mild cognitive impairment score	
Diabetic patients	100.58
Control group	123.35

The mean MCI score was 100.58 in the diabetic group, which was significantly less as compared to 123.35 as seen in the control group. Among 37 patients who had mild cognitive impairment and a score below 110, most patients had problems in calculation and fluency. Object naming test was the least affected. Our study showed that MCI had positive significant correlation ( $p < 0.05$ ) with nephropathy ( $p < 0.05$ ), retinopathy ( $p < 0.05$ ), HbA1c ( $p < 0.05$ ) and duration of DM ( $p < 0.05$ ). There was no significant co-relation between the sex of the patients and MCI ( $p > 0.05$ ) (Table 2).

**Table 2: Relation of mild cognitive impairment with various variables of diabetes mellitus.**

Variable	Positive correlation	p value
Nephropathy	Yes	0.05
Retinopathy	Yes	0.01
HbA1c more than 6.5%	Yes	0.001
Duration of diabetes more than 10 years	Yes	0.05
Gender	No	0.83

## DISCUSSION

Obesity and type 2 diabetes have been associated with an approximately 1.5-fold increased risk of AD.<sup>6</sup> The mechanism by which diabetes may increase dementia risk is uncertain; it does not appear to be mediated entirely through vascular disease. The direct effects of hyperinsulinemia and insulin resistance in the brain, as well as a possible relationship between insulin and amyloid beta metabolism, are areas of active investigation.

Some studies have suggested a role of insulin degrading enzyme (IDE), which metabolizes both amyloid beta and insulin, in the accumulation of oligomeric beta amyloid.<sup>7</sup> Other studies are investigating a pathogenic role for the accumulation of advanced glycation end products within brain tissue.<sup>8</sup> Small pilot studies of intranasal insulin and dietary manipulation in patients with mild cognitive impairment or AD showing improved cognitive function or biochemical profiles provide further support for the potential link between brain insulin and AD pathogenesis.

It is not clear that treating diabetes reduces the risk of dementia. Patients treated with insulin actually had the highest incidence of dementia in a large prospective cohort study, although this was also probably a marker for more severe disease. In a study that randomly assigned 156 older patients with diabetes to two different oral anti-diabetic agents, higher postprandial plasma glucose excursions (less tight diabetes control) were associated with greater declines in cognitive performance measures over one year of follow-up.<sup>9</sup>

An inverse correlation has been noted between some cognitive measures and hemoglobin A1c levels, also suggesting that worse glycemic control may be associated with greater cognitive decline.

However, one study associated a history of severe hypoglycemic episodes with dementia risk among a cohort of patients with type 2 diabetes, suggesting some caution is appropriate in pursuing tight glycemic control in older adults. Cognitive outcomes, as measured by the Digit Symbol Substitution Test, were not different among patients randomized to intensive glycemic control versus usual care in a study subset of the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial when assessed at 40 months into the trial.<sup>10</sup>

This screening battery consists of 8 tests including The mini mental state examination (MMSE) to assess different cognitive functions. The strength of the study lies in the use of a validated cognitive scale developed from a local community based study as the popular western cognitive scales may not be appropriate in our local population as language, culture, education and intelligence are different from the western countries.

## CONCLUSION

There is a strong correlation of MCI with HbA1c. This implies that control of diabetes may help improve cognition and help in better management of diabetes as MCI disrupts the individual's lifestyle and interferes with day-to-day activities. Also as the duration of diabetes and age of the individual increases, MCI worsens.

Hypertension, retinopathy and nephropathy have to be controlled because of their correlation with MCI. This study was a pilot study using a group of 50 patients. A greater sample size will enhance our further understanding regarding MCI and its correlation with diabetes.

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