

# Occurrence Of Severe Cognitive Impairment In Elderly Individuals With Poor Glycemic Control Vs Elderly Individuals With No DM Or Good Glycemic Control: A Case-Control Study

Basma Salman<sup>1</sup>, Fatima Jehangir<sup>2</sup>, Aroosa Jahan<sup>3</sup>, Saira Aslam<sup>4</sup>, Nadra Ansari<sup>5</sup>

## Abstract

**Background:** There is substantial corroboration that diabetes (both T1DM and T2DM) plays an essential role in predisposition to cognitive decline thus leading to dementia in both human and animal studies. <sup>(1,2,3)</sup>. There is a lack of data from our community to support this. We aim to observe the occurrence of cognitive impairment in individuals aged 65 or above with poor glycemic control and compare it with similar age groups of individuals with no DM or good glycemic control. Frailty independently contributes to cognitive decline. We also assessed the frailty index and incorporated it into our result interpretation.

**Methods:** We conducted a case-control study in the primary health care center of Ziauddin University from 1st December 2021 to 30th June 2022. Cases included 83 individuals 65yrs with HbA1c =7 and above and controls included 91 individuals 65yrs and above with HbA1c <7. Both groups were assessed for cognitive decline using the MMSE score and CFS score to determine their dependency status.

**Results:** Moderately uncontrolled Diabetes had the highest association with severe cognitive decline(50%) p-value 0.000 and those who could not manage to do IADLS were severely dementia in our study( p-value 0.046). We also found DM to be associated with high frailty scores. Severely uncontrolled DM was associated with CFS of 5, meaning those dependent on others for instrumental activities of daily living. Those who managed well independently were associated with Pre DM in our study. ( p-value 0.041)

**Conclusion:** Severe cognitive decline has a high association with uncontrolled glycemic control.

**Keywords:** IADLS (instrumental activities of daily living), CFS (chronic frailty scale), MCI (Mild Cognitive Impairment), MMSE (Mini-Mental State Examination), DM (Diabetes Mellitus)

<sup>1</sup> Resident, Ziauddin University; <sup>2</sup> Associate Professor, Ziauddin University; <sup>3</sup> Consultant, Ziauddin University; <sup>4</sup> Resident, Ziauddin University; <sup>5</sup> Resident, Ziauddin University

**Correspondence:** Dr Basma Salman, Resident, Ziauddin University, Karachi. **Email:** drbasmasalman@gmail.com

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## 1. Introduction

Diabetes is a complex metabolic syndrome characterized by elevated levels of blood glucose which leads to serious damage to the heart, brain, blood vessels, eyes, kidneys and nerves over time. According to the International Diabetes Federation, in 2022, 26.7% of adults in Pakistan are affected by diabetes making the total number of cases approximately 33 million. The number continues to rise globally and has been a great source of economic and physical disease burden. It has been established from several studies that Diabetes Mellitus Type 1 and Type 2 play an essential role in contributing to cognitive decline which may lead to dementia over the years. <sup>(1,2,3)</sup>. A review of the literature has suggested that diabetes-related cognitive decline is closely linked to changes within the CNS that are secondary to chronic hyperglycemia. <sup>(4-7)</sup> However its mechanism

is poorly understood but believed to be attributed to a multitude of factors including persistent glucose peaks, cerebral and hippocampal atrophy, increase amyloid metabolism and direct cerebral glucotoxicity. Hypoglycemia has been associated with an increased risk of developing cognitive impairment. <sup>(4)</sup>

Cognitive impairment is a broad term used to describe the analytical integrity of one's brain. However, it is mainly related to memory but is not limited to, and includes comprehension, problem-solving, reasoning as well as decision-making abilities. There are sufficient studies to support that the elderly with DM show an increase in the rate of cognitive decline.

Frailty is a complex state of physical vulnerability attributed to multiple physiological changes. There is transpiring data in the literature to link frailty with cognitive deterioration. In addition, Diabetes impairs cognitive function pathophysiologically similar to

Alzheimer's Dementia thus rendering elderly frail individuals more susceptible.<sup>(3)</sup>

We decided to conduct our study on the prevalence of cognitive impairment in the elderly population because there is a dearth of data on it from Pakistan. Although there are multiple studies done throughout the world associating mild cognitive impairment with DM. Unfortunately, we don't have enough data to establish strong evidence in our population. We aim to establish the association of glycemic control with MCI in the elderly as well as find out its association with the degree of fragility in elderly individuals either with poor or good glycemic control.

## 2. Materials & Methods

A case-control study was conducted in the primary health care center of Ziauddin University, from 1st December 2021 to 30th June 2022. All patients coming to primary care centres aged 65 and above voluntarily willing to participate were enrolled in the study either case (DM or poor glycemic control) or controls (No DM or good glycemic control) with 83 and 91 patients in each group respectively. After taking the informed and voluntary written consent to participate in the study, family physicians asked questions of the subjects and fill the pre-designed questionnaire. Cognitive impairment was assessed using the MMSE score. The chronic Frailty score was used to assess the Frailty index. It evaluates specific domains, including comorbidity, function, and cognition, to generate a frailty score ranging from 1 (very fit) to 9 (terminally ill). Higher scores mean greater risk.

### Inclusion Criteria

The inclusion criteria for cases included any individual aged 65 or more having Type 2 DM with HbA1c > 7 available in the past 3 months. Inclusion criteria for controls are individuals 65 and above with HbA1c < 7 done in the past 3 months of the interview.

### Exclusion criteria

The exclusion criteria were any recent major cardiac or neurological event in the last 6 months like CVA/MI/Malignancy/Mental Illness/COVID-19 requiring hospitalization that may interfere with the mental functioning of the participating individuals, unavailability of recent HbA1c report and patient refusal to participate.

### Tools :

The cognitive impairment will be assessed using the MMSE score.<sup>(18)</sup> Case or control enrolment will be based on their last available HbA1c within the last 3 months. A chronic Frailty score (9 points) was used to assess the Frailty index.

### Limitations:

As we are a resource-limited community we do not have the resources or means to obtain multiple HbA1c or obtain reliable history with evidence. We enrolled case/control based on a single available HbA1c test. It may not pertain to accurate estimation of individuals with controlled DM or no DM. This accounts for the limitation of our study.

### SPSS Analysis:

Data entry was done by using SPSS version 20. Mean and standard deviation was analyzed for numerical variables like age and BMI. Frequency and percentage were computed for categorical variables such as frailty score, MMSE score, HbA1c, and the presence of other co-morbidities. Paired sample t-test was computed for comparing MMSE score and hbA1C. An Independent t-test was computed to see the association of gender with MMSE score. The association of underlying cognitive impairment with variables was analyzed by cross-tabulation and chi-square was computed. P-value < 0.05 was considered significant.

## 3. Results

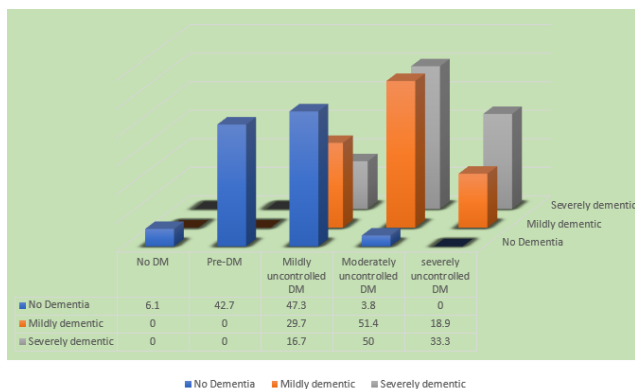
The mean age of the participants was 70.21±5.39 years. On paired sample t-test mean MMSE score was 24.89±2.87, mean hbA1c was 7.2±1.4 with a p-value of 0.000.

The mean Frailty scale was 3.14±0.669. On the independent t-test, the mean of males and females were 25.47±2.65 and 24.21±2.99 respectively showing MMSE score of males was significantly (p-value 0.004) higher as compared to females. Figure one demonstrates the association of glycemic control with the severity of cognitive decline depicting that moderately uncontrolled Diabetes has the highest association with severe cognitive decline (50%) with a p-value of 0.000.

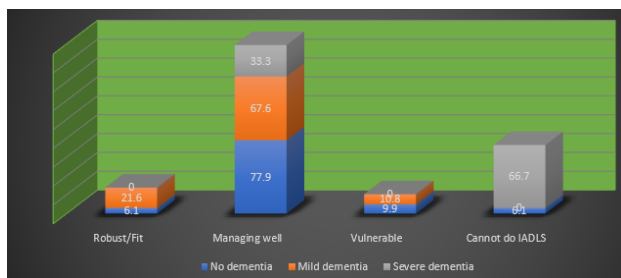
**Table-1** Age of Patients as compared to MMSE score and Frailty scale.

	X±SD	p-value
<b>Age in years</b>	70.21±5.39	
<b>MMSE score</b>	24.89±2.87	0.000
<b>Frailty scale</b>	3.14±0.669	
<b>Gender</b>	Males 25.47±2.65 Females 24.21±2.99	0.004

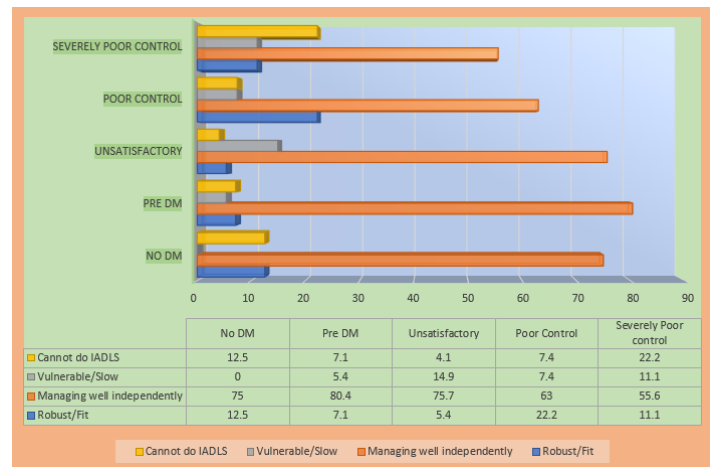
Figure 2 shows the association of frailty with glycemic control. It was seen that those who could not manage to do IADLS were severely dementia in our study. (p-value 0.046) Figure 3 demonstrates the association of frailty with glycemic control. Severely uncontrolled DM was associated with CFS of 5 meaning those who were dependent on others for instrumental activities of daily living and those who were managing well independently were associated with Pre DM in our study. (p-value 0.041).



**Figure-1** Glycemic control association with cognitive decline



**Figure-2** Association of the severity of frailty with the severity of dementia



**Figure-3** Association of frailty with glycemic control

**5. Discussion**

In our study, we compared the MMSE scores of elderly individuals with poor glycemic control to the individuals with good glycemic control or no DM to establish the association of Diabetes and/or poor glycemic control with cognitive decline. It has been suggested in the past from various studies that diabetes (both Type 1 and 2) impairs cognitive function similar to Alzheimer’s mechanism.<sup>(19,20,21)</sup> It has also been postulated earlier that Diabetes causes similar neurodegeneration as dementia.<sup>(3)</sup> Hypoglycemia is presumed to have a direct relationship with cognitive impairment.<sup>(3)</sup>

In our study, we found similar results with poor glycemic controls corresponding to increased cognitive impairment. Thus our study supports that poor glycemic control is associated with mild to moderate degrees of cognitive decline. Interestingly they were also associated with higher degrees of frailty. Large-scale studies in the literature have shown a strong correlation between dementia and Diabetes.<sup>(8-10)</sup> In a recent meta-analysis of 17 studies published in the Scandinavian Journal of primary health care (2020) they found consistent evidence to support DM as an independent risk factor for low cognitive ability in elderly individuals.<sup>(11)</sup> Moreover, our study also links low levels of education to mild to moderate cognitive impairment.

In 2015 research collaboration from Mayo Clinic and Shanghai reported that diabetes-related cognitive impairment was independent of age, gender and co-morbidities.<sup>(13,14,15)</sup> Whereas our study shows slightly higher MMSE scores in males as compared to females (p-value = 0.004). It can be attributed to gender inequality in terms of education and career opportunities prevailing in our society, especially in lower socioeconomic communities.

Frailty is a better predictor of health and functional capacity in elderly diabetics.<sup>(12)</sup> It has been established from several studies that there's an association of cognitive impairment with frailty especially in attention and specialized functions.<sup>(15)</sup> Diabetes contributes to the physical decline of an individual affecting their robustness and energy.<sup>(17)</sup> In our study elderly individuals with high frailty scores showed significant cognitive impairment in both diabetic or poor glycemic control as well as good glycemic control or no DM groups establishing frailty as an independent risk of cognitive impairment. However, we reported in our study that the incidence of severe dementia was associated with high frailty indices. Furthermore, similar to our study another study from Europe has shown increased evidence of Alzheimer's and Vascular dementia in Diabetics particularly individuals with poor glycemic control.<sup>(3,5)</sup> Diabetes increases the risk of vascular as well as Alzheimer's dementia regardless of the age of Diabetes diagnosis.<sup>(7,21,23)</sup> There can be more complex mechanisms involved in the neuro-regulation of glucose metabolism and vascular stressors in the brain. We need further research in the area to understand and alter this mechanism. Another longitudinal cohort study was conducted in the USA in 2007 in which about 900+ participants were studied for a year and individuals with DM were found to have more incidence of MCI similar to our study.<sup>(24)</sup> In addition, it was also evident that individuals with DM had more cerebrovascular accidents and hence vascular dementia was also more prevalent in them.<sup>(25,26,27)</sup> Correspondingly, cognitive impairment has also been linked to individuals with lower educational levels comparable to our study.<sup>(28)</sup> We incidentally found that more robust and fit elderly individuals who had mild cognitive impairment fell into the pre-diabetes criteria.

Further studies are needed to find other factors contributing to these results in our population to

develop a strong causative association between diabetes and cognitive impairment.

## 5. Conclusion

Overall our study establishes a strong association of cognitive impairment with poor glycemic control in elderly individuals in our community. Additionally, individuals with high frailty scores correspond to an increase incidence of cognitive impairment in both DM and non-DM groups affirming that frailty is an independent risk factor for cognitive impairment. Hence we can state that both frailty and poor glycemic control contribute to cognitive decline in the elderly population in our community.

**CONFLICTS OF INTEREST-** None

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**Potential competing interests:** None to report

**Contributions:**

B.S, F.J - Conception of study

B.S, A.J, S.A, N.A - Experimentation/Study conduction

B.S, F.J - Analysis/Interpretation/Discussion

B.S - Manuscript Writing

F.J, A.J, S.A, N.A - Critical Review

B.S - Facilitation and Material analysis

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