Cognitive Impairment Among Older Adults With Diabetes Mellitus in Puducherry: A Community-Based Cross-Sectional Study

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Abstract

Background
Cognitive impairment is a global public health problem in the elderly population. There is increasing evidence that diabetes mellitus predisposes to cognitive impairment. Early diagnosis and management of cognitive impairment can delay the onset of dementia, thereby improving self-care and quality of life of diabetic patients. This study intends to assess cognitive impairment, and the factors influencing cognitive impairment among older adults with diabetes mellitus in Puducherry.

Methods
A community-based cross-sectional study was conducted in field practice areas of a Government Medical College in Puducherry between April and June 2019. After obtaining ethical approval, 240 registered diabetic patients aged 55 years and above were randomly selected. Data on demographic profile and clinical variables were collected using a semi-structured questionnaire. Cognitive function was assessed using the Hindi Mental State Examination (HMSE) tool, and participants who scored below 26 were considered to have cognitive impairment.

Results
Among 240 participants, 67.9% were aged 60 years and above, 62.5% were females, and 83.8% were unemployed. The proportion of cognitive impairment among older adults with diabetes was 30.0% (95% confidence interval (CI): 24.5-36.03). The mean ± standard deviation of the HMSE Score was 26.13 ± 3.8, and the median score was 27. Female gender (P=0.02, adjusted prevalence ratio (aPR) = 5.31, 95% CI: 1.34-21), widowhood status (P=0.005, aPR= 2.71, 95% CI: 1.34-5.46), illiteracy (P<0.001, aPR= 3.55, 95% CI: 1.78-7.07), and presence of probable symptomatic hypoglycemia (P=0.02, aPR= 2.18, 95% CI: 1.13-4.20) were significant predictors of cognitive impairment in the study population by multivariate analysis.

Conclusion
Almost one-third of older adults with diabetes were found to be at risk of cognitive impairment. Older diabetic patients with identified risk factors may be prioritized for a screening of cognitive impairment at the primary care level.

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Results of association was presented as an adjusted prevalence ratio with 95% confidence intervals. The variables that had a significant association in bivariate analysis were entered between each independent variable and cognitive impairment. A \( P \) value of <0.05 was considered statistically significant. The variables that had a significant association in bivariate analysis were entered into the logistic regression model to identify the predictor variables of cognitive impairment. The magnitude of association was presented as an adjusted prevalence ratio with 95% confidence intervals.

Materials And Methods

This community-based descriptive cross-sectional study was conducted between April and June 2019, in the field practice areas of a Government Medical College in Puducherry. The study protocol was approved by the Institute Research Committee and Institute Ethics committee.

Diabetic patients of either gender, aged 55 years and above, registered under non-communicable disease (NCD) clinic in selected health centers were included in the study. Participants who were a known case of neuropsychiatric disorders or on psychoactive drug use and participants who were unable to communicate and follow the investigator’s instructions were excluded from the study.

Presuming the prevalence of cognitive impairment among the older people with diabetes as 63.5% based on a previous study [8], the sample size required at 95% confidence limit, 6.5% absolute precision, and a 10% non-response rate was calculated as 234. A total of 240 study participants, 120 from the Urban Health Training Centre and 120 from the Rural Health Training Centre, were selected.

As the pensionable age in Puducherry is 55 years, participants aged 55 years or above were considered as older adults [7,8]. One hundred and fifty minutes per week or 30 minutes per day for at least five days in a week of moderate-intensity aerobic physical activity was considered as adequate physical activity [9]. The presence of one or more symptoms of hypoglycemia, which gets relieved on taking oral carbohydrates without a test of plasma glucose, in the last 30 days, was the operational definition for probable symptomatic hypoglycemia [10]. For alcohol and tobacco use, the participants were categorized into current, ever, and never users. Current tobacco users were those who consumed tobacco in any form in the last 30 days. Current users of alcohol were those who consumed alcohol in any amount in the last 12 months. The participants who had fasting blood sugar >125 mg/dl and post-prandial blood sugar >200 mg/dl were considered to have uncontrolled diabetes [11]. The body mass index (BMI) criteria for Asians by the regional office for the western pacific region of WHO was used to define underweight (< 18.5 kg/m2), overweight (23 to 24.9 kg/m2), and obesity (≥ 25 kg/m2) among the study participants.

Eligible study participants were randomly selected from the NCD register available in the facility. A home visit was made with the help of a health assistant, auxiliary nurse midwife (ANM), or accredited social health activist (ASHA). After obtaining written informed consent from the study participants, a pre-tested semi-structured questionnaire was used to collect information on the socio-demographic profile and clinical variables. Participants were screened for cognitive impairment using Hindi Mental State Examination (HMSE) tool. Items in the questionnaire were translated forward (English to Tamil) and backward (Tamil to English) by the investigator proficient in both languages. Content validation was done by two public health experts and a psychiatrist.

Hindi Mental State Examination tool was developed by the Indo-US Cross-National Dementia Epidemiology Study. Though the Mini Mental State Examination (MMSE) is the preferred tool for assessing cognitive function, it has few limitations. For the use of the MMSE tool, permission is required, and it can be administered only if the participant is literate [12]. Hence HMSE tool was developed by modifying the Mini Mental State Examination tool and was validated for use in a largely illiterate rural elderly population in India [12]. This tool consists of simple questions and a task, with a maximum score of 30. Participants with a score of less than 26 are considered to have cognitive impairment. They were further classified into mild (score 21-25), moderate (score 11 to 20), or severe (score ≤ 10) based on their scores [13]. Participants with lower scores were referred to a higher center for neuropsychiatric evaluation and further management.

Data were entered in a Microsoft Excel sheet (Microsoft® Corp., Redmond, WA), and data analysis was done using the Statistical Package for Social Sciences (SPSS) software for Windows, version 22.0 (IBM Corp., Armonk, NY). Categorical variables were described as number and percentage, whereas continuous variables were described as mean ± standard deviation (SD). A Chi-square test was applied to identify the association between each independent variable and cognitive impairment. A \( P \)-value of <0.05 was considered statistically significant. The variables that had a significant association in bivariate analysis were entered into the logistic regression model to identify the predictor variables of cognitive impairment. The magnitude of association was presented as an adjusted prevalence ratio with 95% confidence intervals.
Among 240 study participants, 163 (67.9%) were aged 60 years and above. The mean age (±SD) of the study subjects was 63.9 ± 7.1 years. More than one third (38.7%) of the study participants were illiterate, 62.5% were females, and 83.7% were unemployed.

The mean (±SD) of the HMSE Score was 26.13 ± 3.8, and the median HMSE score was 27. The mean HMSE score was 24.2 ± 3.8 for illiterate, 26.1 ± 2.9 for primary level of education, 27.8 ± 4.2 for middle school, and 29.1 ± 1.5 for high school and above.

The proportion of cognitive impairment among older adults with diabetes was 30.0% (95% CI: 24.5-36.03). Out of 240 study subjects assessed using the HMSE tool, 40 (16.7%) study participants had mild cognitive impairment, 31 (12.9%) had moderate, and one participant (0.4%) had severe cognitive impairment (Table 1).

| Variable         | Frequency (n=240) (%) | Cognitive impairment                                                                 |
|------------------|-----------------------|--------------------------------------------------------------------------------------|
| Residence        |                       |                                                                                      |
| Urban            | 120 (50.0)            | Mild (n=40) 21 15 01 Total (n=72) 37 (51.4)                                         |
| Rural            | 120 (50.0)            | 19 16 - 35 (48.6)                                                                  |
| 55-59            | 77 (32.1)             | 05 08 - 13 (18.1)                                                                  |
| 60-69            | 96 (40.0)             | 20 11 - 31 (43.1)                                                                  |
| 70-79            | 58 (24.2)             | 12 09 - 21 (29.2)                                                                  |
| 80-85            | 9 (3.7)               | 03 03 01 07 (9.7)                                                                  |
| Gender           |                       |                                                                                      |
| Male             | 90 (37.5)             | 06 03 - 09 (12.5)                                                                  |
| Female           | 150 (62.5)            | 34 28 01 63 (87.5)                                                                 |
| Marital status   |                       |                                                                                      |
| Married          | 160 (66.7)            | 17 12 - 29 (40.3)                                                                  |
| Widow/widower    | 80 (33.3)             | 23 19 01 43 (59.7)                                                                 |
| Type of family   |                       |                                                                                      |
| Nuclear          | 126 (52.5)            | 20 17 - 37 (51.4)                                                                  |
| Joint            | 114 (47.5)            | 20 14 01 35 (48.6)                                                                 |
| Illiterate       | 93 (38.7)             | 23 25 - 48 (66.7)                                                                  |
| Education        |                       |                                                                                      |
| Primary          | 64 (26.7)             | 13 06 - 19 (26.4)                                                                  |
| Middle           | 47 (19.6)             | 02 - 01 03 (4.2)                                                                   |
| High school & Above | 36 (15.0)     | 02 - - 02 (2.8)                                                                  |
| Unemployed       | 201 (83.8)            | 35 31 1 67 (93.1)                                                                  |
| Employed         | 39 (16.2)             | 05 - - 05 (8.9)                                                                   |

TABLE 1: Distribution of demographic variables and the proportion of cognitive impairment among the study participants (n=240)

Among the respondents, the co-morbidities reported were hypertension (n=138, 57.5%), coronary artery disease (n=24, 10.0%), dyslipidemia (n=12, 5.0%), bronchial asthma (n=10, 4.2%), one old case of pulmonary tuberculosis and one participant was on antiretroviral therapy for HIV. All study subjects had type 2 DM, of which 54.6% had uncontrolled sugar levels. The majority of the study participants (90.4%) were on treatment with oral hypoglycemic agents (OHA). Six participants were on insulin, and 17 (7.1%) were on treatment with both insulin and OHA. The ratio of cognitive impairment was higher among the participants who were on treatment with insulin when compared to those on OHA. Among the eight (3.3%) participants who had a BMI of less than 18.5, seven had cognitive impairment. One hundred sixteen (48.3%) participants had a BMI of more than 25, of which 31 participants had impaired cognition (Table 2).
| Variable                        | Frequency (n=240) (%) | Cognitive impairment |
|--------------------------------|-----------------------|----------------------|
|                                |                       | Mild (n=40)          | Moderate (n=31)  | Severe (n=01) | Total (n=72) (%) |
| Duration of illness            |                       |                      |                    |              |                  |
| < 5 years                      | 113 (47.1)            | 18                   | 15                 | -            | 33 (45.8)        |
| 5-9 years                      | 64 (26.6)             | 10                   | 12                 | -            | 22 (30.6)        |
| ≥ 10 years                     | 63 (26.3)             | 12                   | 4                  | 01           | 17 (23.6)        |
| Co-morbidity                   |                       |                      |                    |              |                  |
| Present                        | 153 (63.8)            | 26                   | 24                 | -            | 50 (69.4)        |
| Absent                         | 87 (36.2)             | 14                   | 07                 | 01           | 22 (30.6)        |
| Treatment                      |                       |                      |                    |              |                  |
| Oral Hypoglycemic Agents       | 217 (90.4)            | 33                   | 30                 | -            | 63 (87.5)        |
| Insulin                        | 06 (2.5)              | 04                   | -                  | 01           | 05 (6.9)         |
| Both                           | 17 (7.1)              | 03                   | 01                 | -            | 04 (5.6)         |
| Probable symptomatic hypoglycemia |                   |                      |                    |              |                  |
| Present                        | 95 (39.6)             | 20                   | 18                 | 01           | 39 (54.2)        |
| Absent                         | 145 (60.4)            | 20                   | 13                 | -            | 33 (45.8)        |
| Blood sugar                    |                       |                      |                    |              |                  |
| Under control                  | 109 (45.4)            | 18                   | 13                 | 01           | 32 (44.4)        |
| Uncontrolled                   | 131 (54.6)            | 22                   | 18                 | -            | 40 (55.6)        |
| Exercise                       |                       |                      |                    |              |                  |
| Adequate                       | 59 (24.6)             | 12                   | 04                 | -            | 16 (22.2)        |
| Inadequate                     | 181 (75.4)            | 28                   | 27                 | 01           | 56 (77.8)        |
| < 18.5                         | 08 (3.3)              | 01                   | 05                 | 01           | 07 (9.7)         |
| 18.5-22.9                      | 66 (27.5)             | 14                   | 04                 | -            | 18 (25.0)        |
| 23-24.9                        | 50 (20.8)             | 10                   | 06                 | -            | 16 (22.2)        |
| 25-29.9                        | 83 (34.6)             | 11                   | 14                 | -            | 25 (34.8)        |
| ≥ 30                           | 33 (13.8)             | 04                   | 02                 | -            | 06 (8.3)         |

**TABLE 2: Distribution of clinical variables and the proportion of cognitive impairment among the study participants**

There was no significant difference in the proportion of cognitive impairment between the urban (30.83%) and rural (29.17%) study subjects (Prevalence ratio= 1.06, 95% CI: 0.62-1.88, P= 0.77). Increasing age, female gender, illiteracy, and unemployment had a significant association with cognitive impairment in bivariate analysis (Table 3).
| Variable         | Frequency n | Cognitive impairment n (%) | Prevalence ratio (95% Confidence Interval) | P-value |
|------------------|-------------|----------------------------|------------------------------------------|---------|
| Residence        |             |                            |                                          |         |
| Urban            | 120         | 37 (30.8)                  | 1.06 (0.72- 1.56)                        | 0.778   |
| Rural            | 120         | 35 (29.2)                  | 1.00 (ref)                               |         |
| Age              |             |                            |                                          |         |
| ≥ 60 years       | 163         | 59 (36.2)                  | 2.14 (1.25- 3.67)                        | 0.002*  |
| <60 years        | 77          | 13 (16.9)                  | 1.00 (ref)                               |         |
| Gender           |             |                            |                                          |         |
| Female           | 150         | 63 (42.0)                  | 4.20 (2.20- 8.03)                        | <0.001* |
| Male             | 90          | 9 (10.0)                   | 1.00 (ref)                               |         |
| Marital status   |             |                            |                                          |         |
| Widow            | 80          | 43 (53.8)                  | 2.97 (2.01- 4.4)                         | <0.001* |
| Married          | 160         | 29 (18.1)                  | 1.00 (ref)                               |         |
| Education        |             |                            |                                          |         |
| Illiterate       | 93          | 48 (51.6)                  | 3.16 (2.09- 4.79)                        | <0.001* |
| Literate         | 147         | 24 (16.3)                  | 1.00 (ref)                               |         |
| Employment       |             |                            |                                          |         |
| Unemployed       | 201         | 67 (33.3)                  | 2.60 (1.12- 6.03)                        | 0.011*  |
| Employed         | 39          | 5 (12.8)                   | 1.00 (ref)                               |         |
| Family type      |             |                            |                                          |         |
| Joint            | 114         | 35 (30.7)                  | 1.05 (0.71- 1.54)                        | 0.821   |
| Nuclear          | 126         | 37 (29.4)                  | 1.00 (ref)                               |         |

**TABLE 3: Association of demographic variables with cognitive impairment (n=240)**

*significant P-value, ref: reference variable

Twenty-eight (11.6%) study participants were current users of tobacco, and 22 (9.2%) study participants were current users of alcohol. Probable symptomatic hypoglycemia and alcohol use had a significant association with cognitive impairment by bivariate analysis. There was no significant association between duration of diabetes and cognitive impairment (Table 4).
| Variable                              | Frequency | Cognitive Impairment present | Prevalence ratio (95% Confidence Interval) | P-value |
|---------------------------------------|-----------|------------------------------|---------------------------------------------|---------|
| Co-morbidity                          |           |                              |                                             |         |
| Present                               | 153       | 50 (32.7)                    | 1.29 (0.84-1.98)                            | 0.230   |
| Absent                                | 87        | 22 (25.3)                    | 1.00 (ref)                                  |         |
| Duration of illness                   |           |                              |                                             |         |
| < 5 years                             | 113       | 33 (29.2)                    | 1.05 (0.71-1.55)                            | 0.800   |
| ≥ 5 years                             | 127       | 39 (30.7)                    | 1.00 (ref)                                  |         |
| Treatment with                        |           |                              |                                             |         |
| Insulin                               | 23        | 9 (39.1)                     | 1.35 (0.78-2.34)                            | 0.315   |
| OHA                                   | 217       | 63 (29.0)                    | 1.00 (ref)                                  |         |
| Probable symptomatic hypoglycemia     |           |                              |                                             |         |
| Present                               | 95        | 39 (41.1)                    | 1.80 (1.22-2.65)                            | 0.002*  |
| Absent                                | 145       | 33 (22.6)                    | 1.00 (ref)                                  |         |
| Tobacco users                         |           |                              |                                             |         |
| Ever                                  | 56        | 19 (33.9)                    | 1.18 (0.77-1.81)                            | 0.464   |
| Never                                 | 184       | 53 (28.8)                    | 1.00 (ref)                                  |         |
| Alcohol users                         |           |                              |                                             |         |
| Ever                                  | 54        | 9 (16.7)                     | 0.49 (0.26-0.92)                            | 0.015*  |
| Never                                 | 186       | 63 (33.9)                    | 1.00 (ref)                                  |         |
| Physical activity                     |           |                              |                                             |         |
| Inadequate                            | 181       | 56 (30.9)                    | 1.14 (0.71-1.83)                            | 0.578   |
| Adequate                              | 59        | 16 (27.1)                    | 1.00 (ref)                                  |         |
| Blood sugar levels                    |           |                              |                                             |         |
| Uncontrolled                          | 131       | 40 (30.5)                    | 1.04 (0.70-1.53)                            | 0.843   |
| Under control                         | 109       | 32 (29.4)                    | 1.00 (ref)                                  |         |
| Body mass index                       |           |                              |                                             |         |
| Malnourished                          | 174       | 54 (31.0)                    | 1.06 (0.71-1.60)                            | 0.570   |
| Normal                                | 66        | 18 (27.3)                    | 1.00 (ref)                                  |         |

**TABLE 4: Association of clinical variables with cognitive impairment (n=240)**

*significant P-value, ref: reference variable, OHA: oral hypoglycemic agents

The variables which had a significant association in bivariate analysis were entered into the logistic regression model. Female gender, widowhood status, illiteracy, and the presence of probable symptomatic hypoglycemia were found to be significant predictors of cognitive impairment in multivariate analysis (Table 5).

| Variable                              | Adjusted Prevalence Ratio | 95% Confidence interval | P value |
|---------------------------------------|---------------------------|-------------------------|---------|
| Age ≥ 60 years                         | 1.96                      | 0.88-4.35               | 0.098   |
| Female gender                         | 5.31                      | 1.34-21                 | 0.017   |
| Widowhood status                      | 2.71                      | 1.34-5.46               | 0.005   |
| Illiterate                            | 3.55                      | 1.78-7.07               | <0.001  |
| Unemployed                            | 0.69                      | 0.18-2.59               | 0.585   |
| Presence of probable symptomatic hypoglycemia | 2.18                  | 1.13-4.20               | 0.019   |
| Alcohol use                           | 2.62                      | 0.66-10.43              | 0.170   |

**TABLE 5: Predictor variables of cognitive impairment on logistic regression analysis**
Discussion

This was a community-based study conducted in the field practice area of the Urban and Rural Health Training Centres of a Government Medical College in Puducherry. The proportion of cognitive impairment in the present study was 30.0%. Other studies reported varied prevalence, 9.6% by Tiwari et al., 10.8% by Krishnamoorthy et al., 33.7% by Khullar et al., 42% by Mukherjee et al., 74% by Pednekar et al. [14-18]. This difference in proportion was probably due to variation in the study population, study tool, and different cut-off scores used for defining the cognitive impairment.

The proportion of cognitive impairment among the study participants below 60 years was 16.8%, between 60 and 80 years was 33.5%, and 80 years or above was 87.5%. The proportion of cognitive impairment in the present study significantly increased with increasing age in bivariate analysis. Research evidence suggests that this association with increasing age might be due to a decline in volume and integrity of white matter and its tract [19].

In the present study, female gender had a significant association with cognitive impairment. Studies have reported that female gender was an independent risk factor for neurocognitive impairment and women with impaired fasting glucose had poor cognitive scores compared to those with normal glucose [16,20]. Genetic predisposition of females due to the presence of apolipoprotein E4 allele, brain-derived neurotrophic factor Met 66 allele, estrogen, the difference in the occupation or educational level in women are probable reasons for the significant association of female gender with cognitive impairment [21].

Widowhood status was found to be a significant predictor of cognitive impairment in the present study. The loss of a spouse is one of the most stressful events for older people. Stress can induce increased glucocorticoid secretion resulting in hippocampal atrophy, resulting in cognitive dysfunction in these individuals [22]. But its association with cognitive impairment in a diabetic individual needs further research.

In this study, illiteracy had a significant association with cognitive impairment. The mean HMSE score was higher in literate than illiterate. Literature states that illiteracy is an independent risk factor for dementia. The high prevalence of dementia in illiterates may be due to poor adaptation to neuropsychological tests and low cognitive reserve [13]. There was a significant association of unemployment with cognitive impairment at the bivariate level, but there was no significant association at the multivariate level. Unemployed elderly might be less physically active than their employed counterparts. Exercise has a direct effect on preserving neurogenesis and favoring neuroplasticity [23]. Studies have reported an association of physical exercise with a decreased risk of cognitive impairment. But these associations in diabetic individuals need to be explored in future research. The present study could not observe a favorable association of physical activity with cognitive impairment. There was no association between the duration of diabetes and cognitive impairment, which was similar to the results obtained in a study by Mukherjee et al. [19].

In the current study, there is a significant association between probable symptomatic hypoglycemia and cognitive impairment. Studies show there is a bidirectional relationship between hypoglycemia and dementia. Acute severe hypoglycemic episodes can lead to chronic subclinical brain damage, cognitive decline, and subsequent dementia [24]. Hyperglycemia mediated advanced glycosylated end-product production, and oxidative stresses can damage neurons and vascular endothelium leading to cognitive dysfunction [5]. Hence strict control of blood sugar plays an important role in the onset of cognitive decline among diabetic patients.

A community-based study using a validated tool appropriate for the local population is the major strength of the study. But HbA1C and blood sugar levels could not be tested due to limited resources. Instead, the latest blood sugar value, preferably tested within the last three months, was considered for knowing whether diabetes is under control. Further, HMSE is a screening tool, and patients with a lower score need further neuropsychiatric evaluation to know the underlying cause and further management.

Conclusions

Almost one-third of older adults with diabetes were found to be at risk of cognitive impairment. Female gender, widowed status, illiteracy, and the presence of probable symptomatic hypoglycemia were found to be significant predictors of cognitive impairment in the diabetic population. Study participants with attributes identified as significant in the current study may be prioritized for the screening of cognitive impairment at the primary care level. Policy-makers should integrate the screening of cognitive impairment along with the identified as significant in the current study may be prioritized for the screening of cognitive impairment at the primary care level. Policy-makers should integrate the screening of cognitive impairment along with the National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases and Stroke (NPCDCS) and also train primary care physicians for screening and providing comprehensive care to individuals with cognitive impairment.

Additional Information

Disclosures
Human subjects: Consent was obtained by all participants in this study. Indira Gandhi Medical College & Research Institute, Institute Ethics Committee (Human Studies) issued approval No. 185/IEC-25/IGMC&RI/F-7/2019. Prior approval for the study was obtained from Indira Gandhi Medical College & Research Institute, Institute Research Committee (Approval No. IRC 2019111), and Institute Ethics Committee (Approval No. 185/IEC-25/IGMC&RI/F-7/2019). Also, written informed consent was obtained from each study participant. Animal subjects: All authors have confirmed that this study did not involve animal subjects or tissue. Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: Payment/services info: All authors have declared that no financial support was received from any organization for the submitted work. Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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