Original Article

Neurovascular Diseases Associated with Type 2 Diabetes Mellitus and Its Impact on Early-Onset Dementia

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ABSTRACT

OBJECTIVE: To investigate the association between neurovascular disorder and early-onset dementia in patients with T2DM, and to assess how dementia severity relates to glycemic control, disease duration, and demographic factors among patients at Liaquat University Hospital, Jamshoro.

METHODOLOGY: A cross-sectional study was conducted in a tertiary care hospital on 112 patients with T2DM. Data was collected regarding age, gender, education, duration of diabetes, and HbA1c levels. Neurovascular complications were confirmed through clinical and radiological evaluation. Cognitive function was assessed using the Mini-Mental State Examination (MMSE), and dementia was diagnosed according to standardized cut-off scores. Statistical analysis was performed using SPSS version 25, with chi-square and Pearson correlation tests used to assess associations among study variables.

RESULTS: Among 112 patients, 58 (51.8%) were male, and 54 (48.2%) were female, with a mean age of 54.6 ± 8.3 years. Neurovascular involvement was present in 46 (41.1%) patients. Dementia was observed in 37 (33%) participants, predominantly among those with disease duration >10 years and poor glycemic control (HbA1c >8%). A major association was found between neurovascular disease and MMSE scores ($p<0.05$).

CONCLUSION: Neurovascular complications in T2DM strongly correlate with early cognitive impairment and dementia, particularly in patients with longer duration and uncontrolled diabetes. Early detection, aggressive glycemic management, and routine neurocognitive screening are necessary to prevent the risk of dementia progression in diabetic patients.

KEYWORDS: Type 2 Diabetes Mellitus, Neurovascular Diseases, Cognitive Decline, Early-Onset Dementia

INTRODUCTION

Neurocognitive conditions (also known as dementia) are chronic and advanced illnesses, characterized by a deterioration of previously established cognition level, adversely affecting social and professional performance[1]. Type 2 Diabetes Mellitus (DM) is a metabolic disorder characterized by insufficiency of beta cells and peripheral insulin resistance, thus contributing to chronic hyperglycemia[2]. Neurovascular complications associated with Type 2 diabetes mellitus are linked to alterations in cognitive function. In type 2 diabetes, cognitive decline primarily impairs memory and understanding, mental strength, and intellectual acuity. Numerous studies have illustrated that the degree of cognitive decline is accelerated with longer duration of type 2 diabetes mellitusx[3]. Additionally, current studies' analysis shows that type 2 diabetes mellitus accelerates the uncertainty of dementia by 1.57 to 2-fold in the general community[4]. Most of the complications associated with type 2 diabetes mellitus, including deranged glucose metabolism and insulin insufficiency leading to microvascular and macrovascular angiopathies, were profoundly involved in the progression of Mild Cognitive Impairment, which in turn accelerates dementia[5]. Type 2 diabetes mellitus is emerging as a global-level pandemic[6]. The worldwide prevalence of diabetes. It is estimated that globally, the prevalence of type 2 diabetes mellitus is approximately 285 million adults, and this figure will increase to 439 million people by the year 2030. Whereas patients with dementia aged 65 years or more have an 80 percent chance of having type 2 diabetes mellitus.2 Several studies show a strong association between type 2 diabetes mellitus and dementia[7]. Along with this global pandemic of metabolic disorders is the emerging challenge of dementia with a longer duration of diabetes. The majority of epidemiological studies to date emphasize type 2 diabetes and dementia, with an increasing risk estimated to be varying between 50% to 100% [8]. Current studies indicate that up to a third of all dementia may be due to risk factors that can be modified, including type 2 diabetesx[9]. Globally, there are more than 18 million dementia patients, and this figure is increasing due to insufficient insight into the pathophysiology behind diabetes and dementia onset[10]. Earlier epidemiological studies had shown that increased HbA1c variability, assessed either through the coefficient of variation (CV) or the standard deviation (SD) of visit-to-visit HbA1c, may be independently associated with an increased risk of

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neurovascular disorders in individuals with type 2 diabetes [11].

In the past few years, various organizations have introduced guidelines for managing elderly patients with diabetes mellitus and dementia. A thorough knowledge of how diabetes and dementia are related may help recognize individuals at high risk of having cognitive impairment and direct healthcare systems to set strategies accordingly for prevention. The objective of this research is to investigate the importance of early onset dementia in type 2 diabetes patients by a cross-sectional method because of its increasing incidence and worldwide prevalence and the subsequent rise in diabetes related complications, including cognitive decline and dementia, which are the topic of concern in this research. This research aims to highlight the significant impact on patients' lives that can hamper their future, the socioeconomic burden, and the resulting decline in the quality of life of these patients. The aim is to investigate techniques that will provide valuable insight into the development of therapeutic techniques, target agents, and drugs to decrease the progression of this particular problem. Getting appropriate information about the relation between type 2 diabetes and early-onset dementia will help to improve the patient's life by providing them with methods for early diagnosis and detection, and it will help the community as a whole by raising awareness among them. It will be of greater help to the healthcare workers as they can review their policies and come up with better preventive measures and management of these patients to prevent the mortality and morbidity of this silent killer disease.

METHODOLOGY

This was a cross-sectional study conducted at a tertiary care hospital on Type 2 Diabetes mellitus (T2DM) to evaluate the relationship between neurovascular complications and early-onset dementia. This study aimed to determine the association among dementia severity, longer duration of diabetes, and increased HbA1c, and various demographic factors. The duration of study was from July to September 2025 at the Medicine Department, Liaquat University Hospital, Jamshoro, a tertiary care teaching hospital affiliated with Liaquat University of Medical and Health Sciences (LUMHS), Jamshoro, Sindh, Pakistan, after approval from the ethical committee. The population of the study includes patients diagnosed with Type 2 Diabetes Mellitus (T2DM) attending the inpatient and outpatient departments of Liaquat University Hospital, Jamshoro. Based on the reported prevalence of 24.4%, d=8%, CI=95%, a total of 112 patients with Type 2 Diabetes Mellitus (T2DM) were included in the study. Eligible individuals who met the study criteria and provided informed consent were selected using a non-probability sampling technique.

The inclusion criteria were patients with Type 2 diabetes mellitus for at least five years, aged 40-65 years, of any gender, and diagnosed with neurovascular problems (clinical and/or radiological).

The Exclusion criteria were Patients with Type 1 Diabetes Mellitus, patients with a history of head injury, stroke unrelated to diabetes mellitus, or pre-existing psychiatric conditions, patients being treated with medication that led to cognitive deficit (e.g., antipsychotics and sedatives), and those who are not willing to participate in the study.

Early-Onset dementia: patients diagnosed with dementia before the age of 65 years.

Assessment of the Neurovascular system: The involvement of the neurovascular system was assessed using clinical and radiological evidence, based of which the presence of neurovascular impairment was established and confirmed.

Type 2 Diabetes Mellitus: The diagnosis of type 2 Diabetes Mellitus was made according to ADA criteria, which state that, for the patient to have type 2 diabetes mellitus, the fasting glucose level must be >126 mg/dL, or the levels of glycosylated haemoglobin (HbA1c) must be ≥6.5%.

For the assessment of cognitive impairment and early onset of dementia, the Mini-Mental State Examination (MMSE) was used, and the scores were categorized as:

Normal cognition: 24-30

Mild cognitive decline: 18-23

Severe cognitive impairment/dementia: <17

For the patient to be labeled as having cognitive decline or dementia, the score should be below the cut-off value.

Patients presenting to the outpatient department of medicine were included in our study after obtaining ethical approval from the Ethical Review Committee (ERC) of Liaquat University of Medical and Health Sciences.

A detailed interview and examination were conducted with each study participant. All the information is taken according to a structured proforma, which consists of demographic information, clinical history, and assessment results.

The process of data collection included the following steps:

Information regarding gender, age, and education level, duration of diabetes, family history, physical activity, and smoking history was recorded.

Blood samples were collected from patients to measure HbA1c levels using standardized laboratory techniques.

Patients were categorized as:

Good control: HbA1c < 7%

Poor control: HbA1c > 7%

Assessment of Neurovascular system: neurovascular involvement was assessed by using clinical and radiological evidence, based on which neurovascular impairment was established and confirmed

Assessment of Clinical signs: weakness, gait disturbance, loss of sensation, and peripheral neuropathy were documented.

Radiological assessment: CT and MRI of the brain confirm the presence of microangiopathic ischemic changes and lacunar infarcts.
The presence or absence of neurovascular disease was documented.
For the analysis and interpretation of data, SPSS was utilized.
For the clinical and demographic variables, descriptive statistics (mean, percentage, frequency, and standard deviation) were used.
The use of the chi-square test was made to determine the correlation between categorical and qualitative variables (that is, cognitive decline, gender of population, and neurovascular disorder).
Finally, for the establishment of an association between the levels of glycosylated hemoglobin or HbA1c, for short duration of disease, which in our case is type 2 Diabetes Mellitus, and MMSE scores.
A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 112 patients diagnosed with Type 2 Diabetes Mellitus (T2DM) were enrolled in this cross-sectional study conducted at Liaquat University Hospital, Jamshoro. Of these, 64 (57.1%) were males, and 48 (42.9%) were females, with a mean age of 54.7 ± 6.8 years (range: 40–65 years).

Demographic Characteristics

The majority of the study participants (61.6%) were from urban areas, while 38.4% belonged to rural areas. The mean duration of diabetes was 9.3 ± 4.7 years, with 58 (51.8%) patients having diabetes for more than 10 years. Family history of diabetes was reported in 69 (61.6%) participants.

Table I:
Demographic Profile of Study Participants (n=112)

	Category	Frequency (n)	Percentage (%)
Gender	Male	64	57.1
	Female	48	42.9
Age (years)	50-40	38	33.9
	60-51	52	46.4
	65-61	22	19.6
Residence	Urban	69	61.6
	Rural	43	38.4
Duration of Diabe-tes (years)	5≥	26	23.2
	10–6	28	25.0
	10<	58	51.8
Family History of Diabetes	Yes	69	61.6
	No	43	38.4

Glycemic Control

The mean HbA1c level among participants was 8.3 ± 1.2%. Based on WHO criteria, 75 (67.0%) patients had poor glycemic control (HbA1c >7%), while 37 (33.0%) had good glycemic control (HbA1c ≤7%).

Table II: Glycemic Control among Study Participants

Glycemic Control (HbA1c)	n	%
%7≥(Good control)	37	33.0
%7<(Poor control)	75	67.0
Mean HbA1c (%)	1.2 ± 8.3	

Prevalence of Neurovascular Disease

Out of 112 T2DM patients, 48 (42.9%) were found to have neurovascular involvement, either peripheral or central, confirmed by clinical and radiological findings. Among these, 30 (62.5%) were males, and 18 (37.5%) were females.

Table III: Distribution of Neurovascular Disease among Participants

Neurovascular Disease	n	%
Present	48	42.9
Absent	64	57.1

Cognitive Status (MMSE Assessment)

The mean Mini-Mental State Examination (MMSE) score was 23.1 ± 3.7. Based on standard cut-offs:
Normal cognition was seen in 54 (48.2%) patients,
Mild cognitive impairment in 36 (32.1%), and Dementia (severe impairment) in 22 (19.6%) participants.

Table IV: Cognitive Function Distribution (Based on MMSE Scores)

Cognitive Category	MMSE Score Range	Frequency (n)	Percentage (%)
Normal cognition	30–24	54	48.2
Mild cognitive impairment	23–18	36	32.1
Dementia / Severe impairment	≥17	22	19.6
Mean MMSE Score	—	23.1±3.7	—

Association between Neurovascular Disease and Dementia

A statistically significant association was observed between neurovascular disease and dementia. Among 48 patients with neurovascular disease, 18 (37.5%) had dementia, compared to only 4 (6.2%) of those without neurovascular involvement ($p < 0.001$).

Correlation between MMSE and Clinical Variables

Pearson's correlation analysis revealed:
Negative correlation between MMSE scores and HbA1c levels ($p = 0.002$),
Negative correlation between MMSE and duration of diabetes ($p < 0.001$), indicating that poor glycemic control and longer disease duration were associated with greater cognitive decline.

Table V: Association between Neurovascular Disease and Cognitive Impairment

Neurovascular Disease	Normal	Mild Impairment	Dementia	Total (n)	p-value
Present	14(29.2%)	16(33.3%)	18(37.5%)	48	>0.001
Absent	40(62.5%)	20(31.3%)	4(6.2%)	64	
Total	54	36	22	112	

Table VI: Correlation between MMSE Score and Clinical Variables

	p-value	Interpretation
HbA1c (%)	0.002	Moderate negative correlation
Duration of Diabetes (yrs)	>0.001	Strong negative correlation
Age (years)	0.011	Mild negative correlation

DISCUSSION

Our study mainly focused on finding out the association between neurovascular disorders and early onset of dementia in type 2 diabetes mellitus (T2DM) patients at Liaquat University Hospital. The results showed a strong association between uncontrolled HbA1C values, long duration of diabetes, neurovascular problems, and cognitive impairment. Dementia was diagnosed in almost one-fifth of participants, and mild cognitive impairment in one-third of participants. These results marked the increasing load of metabolic and neurovascular problems in patients with type 2 diabetes. They stressed the need for population screening and strict management of blood glucose levels.

The total prevalence of cognitive decline (51.7%) in this study aligns with global epidemiological studies, which suggest that 40-60% of diabetic patients experience cognitive problems during their diabetic period [12]. This high prevalence of cognitive decline in T2DM patients may be attributed to long-standing and uncontrolled diabetes, which leads to microvascular ischemia, cerebrovascular insufficiency, and neurodegeneration, leading to impaired neuronal signaling and synaptic plasticity. The documented mean HbA1c level of 8.3% in this study additionally emphasizes the role of uncontrolled diabetes in the progression of cognitive impairment processes.

Several factors demonstrate the pathophysiology linking diabetes to dementia. Peripheral insulin resistance and chronic hyperglycemia, leading to decreased neuronal energy utilization and accumulation of β-amyloid accumulation, impair brain glucose metabolism. Along with vascular insufficiency, cerebrovascular infarcts further exacerbate the damage, leading to "mixed dementia" in T2DM patients[12]. The outcome of this study shows a multifactorial interaction between metabolic and neurovascular components of cognitive decline.

The results of this study show a strong association between the duration of diabetes and dementia. Patients with diabetes with a duration of more than 10 years scored lower in the Mini-Mental State Examination (MMSE) compared to those with shorter durations of disease. This correlation has long been studied and documented in several epidemiological studies, suggesting that longstanding and uncontrolled diabetes and peripheral insulin resistance accelerate cerebrovascular damage and neurodegeneration[13]. Vascular changes and chronic retention of advanced glycation end products (AGEs) lead to deterioration of the blood-brain barrier, resulting in neurovascular insufficiency.

Furthermore, a negative correlation between MMSE scores and HbA1c levels (p = 0.002) was noted, suggesting that individuals with longstanding diabetes had more severe cognitive decline[14]. Similarly, in elderly diabetic patients, with each 1% raised HBA1c levels, there was a considerable cognitive decline. These results emphasize the need for strict blood glucose level control to prevent cognitive and intellectual decline.

Our findings also show resemblance to other studies that show chronic neuropathy and vasculopathy in diabetic patients, which contribute significantly to subcortical vascular dementia and executive dysfunction.

Neurovascular disorders were identified in 42.9% of patients, and a significant proportion (37.5%) of them were found to have dementia. This supports the tentative idea that neurovascular disorder plays a crucial role in facilitating cognitive decline in diabetes[15]. Diabetic vasculopathy, cerebrovascular insufficiency, and microangiopathic changes lead to cerebral hypoperfusion and impair oxygen delivery to neurons, directly resulting in white matter lesions and cortical atrophy.

Gender differences were not statistically significant in this study; however, males had a slightly predominant prevalence of neurovascular disease. Earlier studies show that both genders, male and female, are susceptible to cognitive decline in diabetes; other risk factors may exacerbate the risk[16]. It is evident from our study population that not only gender, but metabolic burden also determines susceptibility to neurocognitive disorders.

These results from a public health perspective are particularly important for developing countries like Pakistan, where the prevalence of Type 2 Diabetes Mellitus is a growing burden, and healthcare facilities remain remarkably limited. Routine cognitive assessment and neurovascular screening in diabetic patients can help identify individuals at high risk for early management. Adapting a healthy lifestyle, strict

monitoring of blood glucose levels, and routine examination of cognitive function can help reduce the risk of cognitive decline in these individuals.

As this was a cross-sectional study, a causal association between diabetes and dementia could not be firmly established. Neurovascular radiological imaging was not uniformly available to all participants. Furthermore, misleading factors such as academic level, depression, and nutritional deficiencies were not properly analyzed. Despite these limitations, the study provides valuable insights into the early recognition of neurocognitive impairment in diabetic patients in a local tertiary care hospital setting.

CONCLUSION

This study highlights a major correlation between neurovascular diseases and early-onset dementia in patients with Type 2 Diabetes Mellitus (T2DM). The findings show that uncontrolled HbA1C, chronic diabetes, and increasing age are strongly correlated with cognitive decline. Patients with evident neurovascular problems, such as stroke or diabetic neuropathy, have profoundly lower Mini-Mental State Examination (MMSE) scores, highlighting the critical role of vascular pathology in diabetes-related cognitive impairment.

The study emphasizes the need for early screening of cognitive decline among T2DM patients, particularly those with uncontrolled blood glucose levels for prolonged periods. Implementing cognitive and neurovascular assessment into routine diabetic care may help identify at-risk individuals and delay the progression of dementia through early management.

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AUTHOR CONTRIBUTION

Memon M: Concept & design of study & proofread
Javeed K: Drafting the article and finalizing the manuscript
Qadeer A: Acquisition of data, grammatical corrections & critical review
Huda N: Revising critically and making it suitable for the final format
Qureshi M: Acquisition of data and topographical review
Memon M: Revision of the manuscript
Kumar S: Final approval

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