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# Older persons with type 2 Diabetes and Depression as a risk factor for Dementia and the mediating role of Inflammation

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***ABSTRACT***
***OBJECTIVE:*** *The purpose of this study is to determine whether depression and dementia are related in type 2 diabetic individuals.*
***METHODS:*** *Patients with clinically confirmed Type 2 diabetes performed Beck's Depression Inventory screening for depression, and the risk of dementia was then determined using medical records, medication information, and death certificates. By evaluating four inflammatory indicators, the mediating role of systemic inflammation was determined (C reactive protein, ESR and Fibrinogen).*
***RESULTS:*** *48 men and 54 women with type 2 diabetes were enrolled in the study, which had 102 individuals. Patients were separated into 90 (88.3%) without depression and 12 (11.7%) with depression (mean ages, 61.86 and 60.9.2, respectively). In depressive patients, the mean BMI was 33.5 9.3, whereas in non-depressive individuals, it was 31.9 8.9. (P value 0.01). When it came to the existence of hypertension, hyperlipidemia, and smoking as dementia risk factors, there were no appreciable differences between patients with and without depression. When compared to individuals without depression, patients with depression showed considerably lower overall MoCA scores (23.21 3.48 vs. 26.34 3.78, P 0.05) and severe cognitive impairment. Diabetes was a serious complication in persons with depression who also had neuropathy (P value 0.005). Other complications as diabetic retinopathy and nephropathy were non-significant. Inflammatory markers levels in patients with depressive symptoms were significantly higher (P value < 0.01).*
***CONCLUSION:*** *In patients with type 2 diabetes, there is an important association between dementia and depression. Systemic inflammation had a significant role in the relation between depression and dementia.*
***KEYWORDS:*** *Depression; Dementia; dm; Inflammatory Markers*

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## I. Introduction

Depression is a common, serious depressive condition that affects patients' emotions and behaviour. It can be treated, although it does cause a loss of interest in formerly enjoyable activities. Economic and social upheaval are the results [1]. The two illnesses that affect older persons the most frequently are diabetes mellitus and depression. The link between the two diseases is crucial because diabetes raises the likelihood of depression in individuals with diabetes and vice versa [2]. The primary issue with these disorders is the slow diagnosis [3]. As a result, those patients receive a diagnosis that is too late because the disease is already advanced [4]. Recent research found that diabetes and depression each separately raise the risk of dementia [5]. Patients with diabetes were more likely to develop any form of dementia, but especially Alzheimer disease (AD). Along with other dementia factors, depression also doubled the chance of AD [6]. Type 2 DM and dementia both exhibit inflammatory symptoms as well as abnormal insulin pathways [7]. It must be concentrated on [8] since the relationship between the metabolism of beta amyloid and tau proteins has not yet been described. Although there is a high correlation between depression and dementia—by approximately 50%, especially in AD—it is unclear whether depression causes dementia or develops as a result of it. The presence of amyloid and tau signals in AD may explain elderly people with depressive symptoms [9]. Therefore, depressed symptoms could be a precursor to dementia, which is being utilised to manage and prevent dementia in the elderly [9].

## II. PATIENTS AND METHODS

Self-Rating Depression Scale was used to assess depression in 102 type-2 diabetic patients who visit the outpatient clinic Hospital. Patients were divided into two groups using the Zung Self-Rating Depression Scale

(ZSDS), with the first group having normal ZSDS scores (less than 50) and the second group having ZSDS scores (equal to or greater than 50). (figure 1).

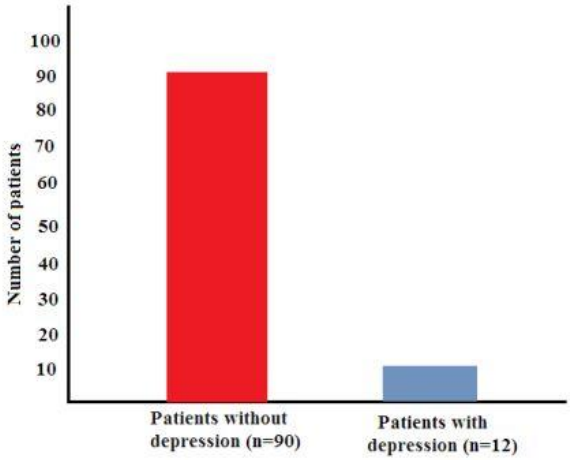


**FIGURE 1:** Classification of patients according to Zung Self-Rating Depression Scale (ZSDS)

A written informed consent form was signed by all patients and/or their family members. Patients having recent prescriptions for medications that may affect cognitive functioning (such as antidepressants and antipsychotics) and those with a history of drug abuse or alcoholism were also excluded. Patients with psycho-neurological illnesses were also not allowed to participate. According to the MoCA, the clinical presentation and symptoms of these patients' dementia were evaluated. The key domains of the MoCA scale are attention, executive functions, memory, language, attention, naming, visual-spatial skills, and orientation. There have been 30 points scored altogether. If the MoCA score is 25 points or less, the cognition is deemed compromised [10]. Venous blood samples were assayed for plasma C-reactive protein (CRP). erythrocyte sedimentation rate (ESR) and fibrinogen using a high-sensitivity immunonephelometric assay.

**STATISTICAL ANALYSIS**

Data and results from the current study were examined using IBM SPSS version 21. While categorical data were expressed as percentages and numbers, continuous data were expressed as mean SD. The chisquare test was used to assess categorical data, while the Student's t test was employed to analyse continuous data. In cases where the data had an excessively uneven distribution, the Mann-Whitney test was utilised to compare the two groups.

## III. Results

102 participants with Type 2 Diabetes who had received a clinical diagnosis participated in the trial; 48 of them were men and 54 were women. According to depression detection, patients were divided into 90 patients without depression (48.9 percent males and 51.1 percent females) and 12 patients with depression (mean age standard deviation: 618.6, 60.99.2), respectively. Of the 90 patients without depression, 33.3 percent of whom were male and 66.7 percent of whom were female. There were 12 patients in the sampled group with depressive symptoms; 1 (8.3 percent) were single, 8 (66.7 percent) were married, and 3 (25 percent) were widowed. There were 90 patients without depression, of whom 7 (7.8%) were single, 71 (78.9%) were married, and 12 (13.3%) were widowed. The patient's occupation and educational background were not statistically significant. In depressive patients, the mean BMI was 33.5 9.3, but in non-depressive patients, it was 31.9 8.9. (P = 0.01) (Table 1).

According to Table 2, those with depression had significantly worse cognition than people without depression, and their overall MoCA scores were also significantly lower (23.21 3.48 vs. 26.34 3.78, P 0.05). The MoCA test's memory, executive functions, naming, and attention were the key areas where there were severe impairments. In contrast to patients without depression, patients with depression had slightly lower scores in the language, orientation, and visual-spatial skill categories.

In our analysis, hypertension was the most common risk factor for dementia, occurring in 5 (41%) of the depressed patients and 35 (38.9%) of the non-depressed individuals. Hyperlipidemia, which was found in 35 (38.9 percent) patients without depression and 2 (16.6 percent) cases with depression, was the second most common risk factor. Smoking was found in 2 (25 percent) cases with depression and 13 (13.8 percent) instances without depression. Regarding the presence of hypertension, hyperlipidemia, and smoking as dementia risk factors, there was no discernible difference between patients with and without depression (Table 3). According

to the study group, the average duration of DM was 9.1 2.9 years for cases without depression and 8.5 3.6 years for individuals with depression. Only two (16.6%) cases of depression were treated by diet control, four (33.2%) by oral medicines, and six (50%) by insulin. Patients who were not depressed received oral treatment in 46.1% of cases, insulin in 25% of cases, and diet control alone in 19.1% of cases (P value 0.01). Mean HbA1c mg% in diabetic individuals with depression was 8.1 1.9, compared to 6.8 2.2 in patients without depression (P value 0.01). Diabetes complications include neuropathy, which is present in 6 (50%) of the patients with depression and 25 (27.8%) of the patients without depression in our sample of patients (P value 0.005). Nephropathy and diabetic retinopathy were unimportant additional problems (Table4). In our study, patients with a diagnosis of depression had inflammatory marker levels of ESR (34.5 ± 30.6 mm/h), CRP (7.12 ± 3.45), and fibrinogen level (791.6 ± 228.8). However, in patients without depression, indicators levels were ESR (18.3 ± 19.1 mm/h), CRP (4.1 ± 1.1), and Fibrinogen level (683.7 ± 214.2) (P value < 0.01). (Table 5).

| **Socio -demographic data** | **Cases with depression (n=12)** | **Cases without depression (n=90)** | **p-value** |
|---|---|---|---|
| **Age / years** | | | |
| Mean ± SD | 61.5 ± 8.6 | 60.9 ± 9.2 | NS |
| **Sex** | | | |
| Male | 4 (33.3%) | 44 (48.9%) | 0.01 |
| Female | 8 (66.7%) | 46 (51.1%) | |
| **Marital status** | | | |
| Single | 1 (8.3%) | 7 (7.8%) | NS |
| Married | 8 (66.7%) | 71 (78.9%) | |
| Widowed | 3 (25%) | 12 (13.3%) | |
| **Occupation** | | | |
| Non worker/housewife | 3 (25%) | 19 (21.1%) | |
| Office worker | 4 (33.3%) | 41 (45.6%) | NS |
| Manual worker | 4 (33.3%) | 21 (23.3%) | |
| Retired | 1 (8.3%) | 9 (10%) | |
| **Education** | | | |
| Non-educated | 2 (16.6%) | 9 (10%) | NS |
| Primary/Secondary school | 4 (33.3%) | 21 (23.3%) | |
| Tertiary school | | | |
| University education | 4 (33.3%) | 25 (27.8%) | |
| | 2 (16.6%) | 35 (38.9%) | |
| **Mean BMI (SD)** | 33.5 ± 9.3 | 31.9 ± 8.9 | 0.01 |

**TABLE 1 :** Socio-demographic data among studied groups

| | **Preserved Cognition** | **Impaired Cognition** | **P-Value** |
|---|---|---|---|
| **MoCA test scores** | | | |
| Visual-spatial ability | 3.64 ± 1.07 | 3.35 ± 1.23 | 0.47 |
| Naming | 2.47 ± 0.52 | 2.19 ± 0.41 | P <0.05* |
| Executive functions | 3.42 ± 0.54 | 2.53 ± 1.29 | P <0.05* |
| Attention | 4.31 ± 0.69 | 3.76 ± 1.25 | 0.01 * |
| Language | 2.66 ± 0.23 | 2.41 ± 0.54 | 0.08 |
| Memory | 4.32 ± 0.68 | 3.46 ± 1.17 | P <0.005* |
| Orientation | 5.13 ± 0.55 | 4.96 ± 0.98 | P= 0.09 |
| Total MoCA score | 26.09 ± 3.68 | 22.14 ± 4.32 | P<0.005* |

**TABLE 2 :** Cognitive impairment among studied patients

| **Risk factors** | **Cases with depression (n=12)** | **Cases without depression (n=90)** | **p-value** |
|---|---|---|---|
| **Smoking** | | | |
| Yes | 2 (25%) | 13 (13.8%) | NS |
| No | 6 (75%) | 81 (86.2%) | |
| **Hypertension** | | | |
| Yes | 5 (41.7%) | 35 (38.9%) | NS |
| No | 7 (58.3%) | 55 (61.1%) | |
| **Hyperlipidemia** | | | |
| Yes | 2 (16.6%) | 18 (20%) | NS |
| No | 10 (83.4%) | 72 (80%) | |

**TABLE 3:** Risk factors for dementia

| Variable | Cases with depression (n=12) | Cases without depression (n=90) | p-value |
|---|---|---|---|
| **Duration of DM** | 8.5 ± 3.6 | 9.1 ± 2.9 | NS |
| **Treatment of DM** | | | |
| Diet control only | 2 (16.6%) | 19 (21.1%) | 0.01 |
| Oral medication | 4 (33.2%) | 46 (51.1%) | |
| Insulin | 6 (50%) | 25 (27.8%) | |
| **Mean HbA1c mg% (SD)** | 8.1 ± 1.9 | 6.8 ± 2.2 | 0.01 |
| **Neuropathy** | | | |
| Yes | 6 (50%) | 25 (27.8%) | 0.005 |
| No | 6 (50%) | 65 (72.2%) | |
| **Diabetic retinopathy** | | | |
| Yes | 2 (16.6%) | 19 (21.1%) | NS |
| No | 10 (83.4%) | 71 (78.9%) | |
| **Diabetic nephropathy** | | | |
| Yes | 1 (8.3%) | 9 (10%) | NS |
| No | 11 (91.7%) | 81 (90%) | |

**TABLE 4 :** Duration, medication, and complication of DM among studied groups

| Markers of inflammation | Cases with depression (n=12) | Cases without depression (n=90) | p-value |
|---|---|---|---|
| **ESR (mm/h)** | 34.5 ± 30.6 | 18.3 ± 19.1 | P < 0.01 |
| **CRP** | 7.12 ± 3.45 | 4.1 ± 1.1 | P < 0.01 |
| **Fibrinogen** | 791.6 ± 228.8 | 683.7 ± 214.2 | P < 0.01 |

**TABLE 5 :** Levels of markers of inflammation

## IV. Discussion

In this study, we looked at 102 patients with type 2 diabetes and used the Beck Depression Scale to measure comorbid depression, dementia symptoms, and the function of inflammatory marker expression in these patients. According to our findings, type 2 diabetic patients had a higher incidence of depression than people of a similar age and sex from the general population. This is consistent with the majority of studies evaluating depression in diabetic patients [11] and is primarily due to the microvascular damage to the brain, poor control, and related factors like increased BMI. Other studies raised the contentious possibility that depressive symptoms could be the first signs of cognitive impairment in dementia patients and be regarded as prodromal symptoms of dementia [13].

Therefore, it is not considered to be a typical epidemiological finding. However, there are numerous theories and justifications that link depression to being a risk factor for dementia, as well as numerous scientific processes, such as anomalies in the hypothalamic-pituitary axis identified in depressed people [14]. Depression has been associated with dysregulation of the hypothalamic-pituitary axis, which has been shown to increase glucocorticoid production and impair negative feedback, resulting in abnormal cortisol levels that harm cognition-related brain regions like the hypothalamus [15] and decrease neurogenesis in important brain regions [16]. Also, patients with both DM and depression show a double increase in developing cardiovascular risk factors which may be attributed to develop symptoms of dementia of vascular origin [17].

We discovered a correlation between depressions in type 2 diabetic patients and elevated inflammatory indicators in our cross-sectional assessment of inflammatory markers (CRP, ESR, Fibrinogen). Compared to patients with DM alone, individuals with depression and DM were found to have significantly higher fibrinogen levels in other research, with CRP being the most frequently analyzed inflammatory measure that significantly correlated with depression in type 2 DM, similar to our findings [18,19]. We can thus demonstrate that depression is associated with higher levels of inflammatory markers in older diabetes persons. The levels of inflammatory mediators in these sad persons are also influenced by MCI. According to our findings, patients with depression had much worse cognition than those without depression, and their overall MoCA scores were also significantly lower. The MoCA test's memory, executive functions, naming, and attention were the key areas where there were severe impairments. In contrast to patients without depression, patients with depression had slightly lower scores in the language, orientation, and visual-spatial skill categories.

Researchers are interested in how diabetes affects cognitive function since studies have connected chronic hyperglycemia [22] and recurrent episodes of severe hypoglycemia [23] to cognitive decline in type 1 diabetes patients. Numerous investigations have shown a connection between type 2 diabetes and cognitive decline [24, 25]. However, Strachan et al. [26] recently debunked this alleged association, concluding that the studies' findings were significantly different in terms of the diabetes population they looked at and the psychological tests they employed. The relationship between type 2 diabetes mellitus and cognitive function is complex because additional comorbidities frequently associated with the condition, such as cardiovascular

disease, hypertension, and depression, are also associated with cognitive deficits. Extra neuronal hyperglycemia, disturbed brain insulin signalling [27], disordered brain glucose metabolism, and challenges brought on by likely elevated cortisol levels have all been proposed as potential mechanisms relating type 2 diabetes to cognitive impairment.

Comorbid depression is becoming more widely recognized as an important component of high-quality clinical care for patients with chronic medical illnesses in specialty medical settings, particularly in the

geriatric population. Diabetes is one of the chronic medical disorders with the highest psychological and behavioral demands [28]; comorbid depression in diabetes can lead to poorer results and an increased risk of complications by reducing adherence to glucose monitoring, exercise, food, and medication regimes.

## V. Conclusion

In patients with type 2 diabetes, there is an important association between dementia and depression as risk factors. Systemic inflammation had no role in relation between depression and dementia.

## Acknowledgement

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**CONFLICT OF INTEREST**

The author declare that there are no conflicts of interest.

**DATA AND MATERIALS AVAIBILITY**

All data associated with this study are present in the paper.

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