Original Research Article

Depression as a risk factor for dementia in older people with type 2 diabetes and the mediating effect of inflammation

Abstract

Objective: The aim of this study is to detect the relation between depression and dementia in patients with type 2 diabetes.

Methods: Clinically diagnosed Type 2 diabetes underwent screening for depression using Beck's Depression Inventory scale and subsequent risk of dementia defined using medical reports, prescription data and death certificates. The mediating act of inflammation systemically was measured by assessing four inflammatory markers (C reactive protein, ESR and Fibrinogen).

Results: The study was conducted on 102 diabetic type 2 patients, included 48 males and 54 females. Patients divided into 12 (11.7%) patients with depression and 90 (88.3%) patients without depression (mean age 61±8.6 and 60.9±9.2 respectively). Mean BMI in depressive patients was 33.5 ± 9.3 and was 31.9 ± 8.9 in non-depressive cases (P value 0.01). There were no significant differences in patients with and without depression regarding the presence of hypertension, hyperlipidemia and smoking as risk factors of dementia. Patients with depression had significant impaired cognition and the total MoCA scores were significantly lower than those of patients without depression (23.21 ± 3.48 vs 26.34 ± 3.78, P <0.05). Complication of diabetes in patients with depression as neuropathy was significant (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.

Key words

Depression, Dementia, DM, Inflammatory markers

1. Introduction

Depression is a frequent important negative disorder disturbing patient`s feelings and behavior. However it is treatable condition, it leads to loss of interest in previous enjoyable stuff. It leads to economic and social disruption (1).

Diabetes mellitus and depression are the most common diseases in old age patients. The relation of the two diseases is very important, as depression in young patients increase possibility of diabetes and diabetes in adults increases depression risk (2).

The main problem of these diseases is the late detection (3). Therefore, those patients are diagnosed too late when the disease is already in late stages (4). Recent studies determined that both depression and diabetes independently increase the risk of dementia (5). Diabetic patients had a higher risk of all types of dementia mainly Alzheimer disease (AD). Depression also had a double risk of AD occurrence as well as other dementia causes (6).

Dementia and type 2 DM share manifestations as inflammation and also disturbed insulin mechanisms (7). The relation between metabolism of beta amyloid and tau proteins has not explained till now, so it must be focused at (8). Depression and anxiety had a strong relation to dementia by almost 50 %, especially to AD, but without knowing the exact link between them either depression leads to dementia or occur as a result of it. In old patients with depressive symptoms, it could be explained by presence of amyloid and tau signs in AD (9). So, depressive manifestations could be an early signs of dementia, which used now in prevention and management of dementia in elderly (9).

2. PATIENTS AND METHODS

Our study was conducted on 102 patients with type-2 DM who attend the outpatient clinic of Mansoura University hospital from which depression was assessed by using the Arabic version of the Zung Self-Rating Depression Scale which is valid, reliable, and be useful tool for Arabic-speaking patients. By Zung Self-Rating Depression Scale (ZSDS) patients were classified into two groups: first group was patients with normal ZSDS (score less than 50) and the second group with ZSDS (score equal to or more than 50) (**figure 1)**.

All patients or their relatives signed a written informed consent form. The Institutional Review Board of Mansoura University's Faculty of Medicine approved the study.

Patients with psycho-neurological diseases, those on recent prescriptions that may influence cognitive functioning (such as antidepressants and antipsychotic medicines), and those with a history of drug misuse or alcoholic were excluded.

Dementia in these patients was assessed by the clinical presentation and symptoms according to the MoCA. Attention, executive functions, memory, language, attention, naming, visual-spatial skills, and orientation are the major domains of the MoCA scale. A total of 30 points has been scored. The cognition is considered compromised if MoCA score is 25 points or less [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

The current study's data and findings were analyzed using IBM SPSS version 21.

Continuous data were expressed as mean SD, whereas categorical data were expressed as numbers and percentages.

The Student's t test was used to compare continuous data, whereas the chi-square test was used to evaluate categorical data.

The Mann–Whitney test was used to compare the two groups when the data was abnormally distributed.

3. Results

The study was conducted on 102 clinically diagnosed Type 2 Diabetes patients 48 of them were male and 54 were female. Patients were classified according to depression detection into 12 patients with depression (33.3% males and 66.7 % females) and 90 patients without (48.9% males and 51.1% females) (P value 0.01) with (mean age ± standard deviation) (61±8.6), (60.9±9.2) respectively. As regard marital status of selected group of patients, with depressive symptoms, there were 12 patients (1 (8.3%) was single, 8 (66.7%) were married and 3 (25%) were widowed). Patients with no depression were 90 (7 (7.8%) were single, 71 (78.9%) were married and 12 (13.3%) were widowed). Patient's occupation and education levels were not significant statistically. Mean BMI in depressive patients was 33.5 ± 9.3 and was 31.9 ± 8.9 in non-depressive cases (P value 0.01) (Table 1).

Table 2 demonstrated that patients with depression had significant impaired cognition and the total MoCA scores were significantly lower than those of patients without depression (23.21 ± 3.48 vs 26.34 ± 3.78, P <0.05). The main domains of MoCA test that show significant impairments were memory, executive functions, naming, and attention. While the domains of the visual-spatial ability, language, and orientation were slightly decreased in patients with depression compared with patients without depression.

Hypertension was the most frequent risk factor of dementia in our study, occurring in 5 (41%) depressive patients and in 35 (38.9%) non depressive patients. The second most frequent risk factor was hyperlipidemia (in 2 (16.6%) cases with depression and in 35 (38.9%) cases without), followed by smoking which detected in 2 (25%) cases

with depression and in 13 (13.8%) non depressive cases. There were no significant difference in patients with and without depression regarding the presence of hypertension, hyperlipidemia and smoking as a risk factors of dementia (Table 3).

According to duration of DM among studied group, cases with depression were 8.5 ± 3.6 years and cases without depression were 9.1 ± 2.9 years with no significant difference. Only 2 (16.6%) cases with depression treated by diet control, 4 (33.2%) cases by oral medications and 6 (50%) cases by insulin. In patients without depression, 19 (21.1%) of them were on diet control only, 46 (51.1%) were on oral therapy and 25 (27.8%) were on insulin (P value 0.01). Mean HbA1c mg% in diabetic patients associated with depression was 8.1 ± 1.9 while in patients not associated with depression was 6.8 ± 2.2 (P value 0.01). Complications of diabetes in our selected patients as neuropathy present in 6 (50%) patients with depression and in 25 (27.8%) patients without depression (P value 0.005). Other complications as diabetic retinopathy and nephropathy were non-significant (Table4).

Inflammatory markers levels in patients diagnosed with depression in our study were ESR (34.5 ± 30.6 mm/h), CRP (7.12 ± 3.45), and Fibrinogen level (791.6 ± 228.8). In the other hand markers levels were ESR (18.3 ± 19.1 mm/h), CRP (4.1 ± 1.1), and Fibrinogen level (683.7 ± 214.2) in cases without depression (P value < 0.01) (Table 5).

4. Discussion

In our study we investigated 102 patients with type2 DM assessing the comorbid depression in these patients using Beck's Depression Scale, symptoms of dementia and the role of inflammatory markers expression in these patients.

In our findings, the incidence of depression was higher in patients with type 2 DM compared to normal population matched age and sex which is co existent with most of trials assessing depression in diabetic patients (11) which is mainly attributed to the micro vascular affection of the brain, poor control and associated factors like increased BMI.

Depression is a recognized risk factor for dementia in the older population, people with diabetes, a group at higher risk of dementia than the general population (12), so in our study we suggest increased dementia risk in patients with type 2 DM with coincident depression, in controversial opinion to these findings, other trials noted that depressive symptoms may be the initial presentations of cognitive impairment in dementia patients considered as prodromal symptoms of dementia (13). So it's not attributed as common epidemiological findings. But there are many hypothesis and explanations that Link depression to be a risk factor for dementia and many biological mechanisms as abnormalities in hypothalamic-pituitary axis found in patients with depression (14). Dysregulation of the hypothalamicpituitary axis found in depression has been linked to higher glucocorticoid production and impaired negative feedback leading to abnormal cortisol level damaging brain areas involved in cognition such as the hypothalamus (15) as well as decrease neurogenesis in key brain areas (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).

In our cross sectional assessment of inflammatory markers we found association between depressions in type 2 Diabetic patients and raised inflammatory markers (CRP, ESR, Fibrinogen). In other studies CRP was the most commonly examined inflammatory marker that shows significant association with depression in type2 DM like our findings (18,19), while there are minimal studies that showed significant increased fibrinogen level in patients with depression & DM, when compared with patients having DM without depression (20). As a result, we can show that depression is connected with greater levels of inflammatory markers in diabetic older individuals.

MCI has an additional influence on the levels of inflammatory mediators in these depressed people.

Our results demonstrated that patients with depression had significant impaired cognition and the total MoCA scores were significantly lower than those of patients without depression. The main domains of MoCA test that show significant impairments were memory, executive functions, naming, and attention. While the domains of the visual-spatial ability, language, and orientation were slightly decreased in patients with depression compared with patients without depression.

The influence of diabetes on cognitive function has piqued researchers' curiosity, as studies have linked chronic hyperglycemia (22) and recurring bouts of severe hypoglycemia (23) to cognitive deterioration in type 1 diabetes patients.Type 2 diabetes has also been linked to cognitive impairment, according to numerous studies (24, 25). However, Strachan et al (26) recently refuted this assumed link, finding in their study that the researches differ greatly in terms of the diabetes population investigated and the psychological measures utilized.

Because other comorbidities commonly linked with type 2 diabetes mellitus, such as cardiovascular disease, hypertension, and depression, all are also related with cognitive deficiency, the link between diabetes mellitus and cognitive function is difficult to understand. Extraneuronal hyperglycemia, disrupted brain glucose metabolism, altered brain insulin signaling (27), and difficulties secondary to probable hypercortisolemia have all been suggested as possible mechanisms linking type2 diabetes to impaired cognition.

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.

5. 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.

Ethical approval

The study was approved by the Medical Ethics Committee of Mansoura University.

Data and materials availability

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

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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Figure 1: classification of patients according to Zung Self-Rating Depression Scale (ZSDS)

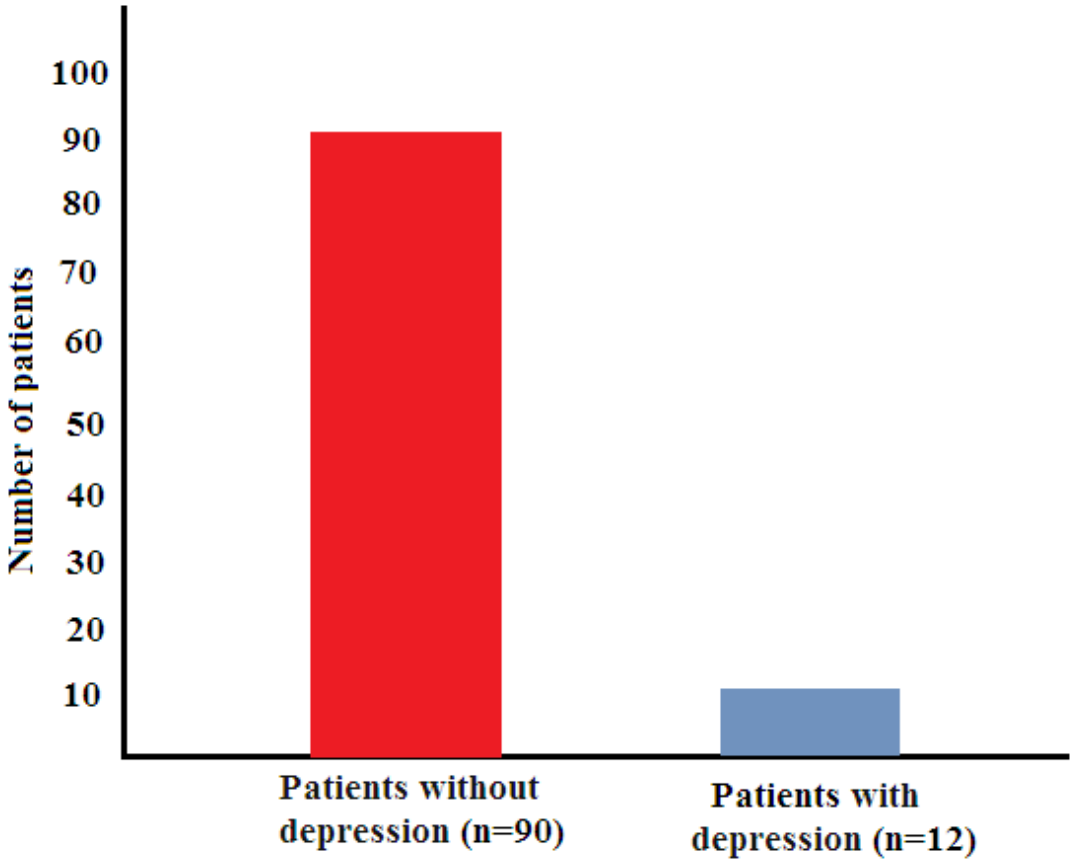

Table 1: Socio-demographic data among studied groups

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%)	
Primary /Secondary school	4 (33.3%)	21 (23.3%)	NS
Tertiary school	4 (33.3%)	25 (27.8%)	
University education	2 (16.6%)	35 (38.9%)	
Mean BMI (SD)	33.5 ± 9.3	31.9 ± 8.9	0.01

Table 2: Cognitive impairment among studied patients

	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 3: Risk factors for dementia

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

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 5: Levels of markers of inflamation

Markers of inflamation	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