

A COMPREHENSIVE REVIEW ON DEPRESSION IN DIABETIC PATIENTS

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ABSTRACT

Diabetes mellitus (DM) is a frequently experienced metabolic disease with chronic features and involves numerous complications around its course, which causes severe restriction and disability in an individual's common life. It was stated that the incidence of depression is higher in diabetic patients and that diabetes is one of the risk factors in the development of depression. Depression has been shown to be correlated with poor self-management (adherence to diet and medication, physical exercise, and monitoring of blood glucose levels) and high HbA1C levels. The main intention of this article is to produce a comprehensive review of epidemiological findings, clinical attentions, and management approaches concerning depression in patients with DM.

Keywords: Diabetes mellitus, Depression, Comorbidity, Complications, Self-care.

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INTRODUCTION

The elevating stress of diabetes among adults (aged 20-70 years) is a major public health concern worldwide [1]. The number of diabetic patients is assumed to rise from 135 million in 1995 to 300 million in 2025. Developing countries are expected to behold a 170% increase in the prevalence of diabetes correlated to 42% increase in developed countries. In 2025, over 75% of people having diabetes globally will be living in developing countries [2]. Particularly the prevalence of diabetes between Asian populations is increasing rapidly, compelled largely by economic development, nutrition transition, and torpid lifestyles. In 2007, around 110 million individuals were affected with diabetes in Asia, with a young and middle-aged population that is affected excessively [3].

Type 2 diabetes mellitus (T2DM) states for the majority of all diabetes cases. T2DM has a number of incessant effects, including disability, cardiovascular disease (CVD), kidney disease, cataract, and blindness [1]. T2DM is also associated with clear decline in the quality of life (QOL) [4]. Comorbid depression, in addition, will reduce the QOL in people with T2DM [5], and is associated with poor treatment outcomes and lowered glycemic control [6,7]. Prevalence of depression is two-fold in people with T2DM compared to those without [8].

Depressive symptoms may thus be an important element of QOL in diabetes. Therefore, a study on the effect of depressive symptoms on QOL in individuals with diabetes is justified. This systematic review intent to explain this knowledge on the association of depressive symptoms with various forms of QOL in individuals with diabetes.

The intention of this review is to bring to light the presently available proof about some aspects of the co-occurrence of the two trembled diseases, namely, depression and diabetes, as both are frequently sustained together in regular clinical practice. The review largely centralized on the association of depression with poor glycemic control and diabetic complications as these are the determinants that have been found to form a fertile ground for the abandoned cycle of one leading to and exacerbating the other and poor control of either depression or diabetes when both exist together.

DIABETES AND DEPRESSION: THE BI-DIRECTIONAL ASSOCIATION

The association has been well established in diverse studies. The presence of diabetes approximately doubles the odds of comorbid

depression, and this is observed across an ethnically different group of people [9]. The general risk estimate discerns across community and clinical settings regardless of differences in prevalence rates between these settings. Hence, the clinicians and the epidemiologists can cast individuals with diabetes to be twice as liable to be depressed as otherwise similar nondiabetic individuals [10]. Still, it has been noted that several factors stated to be linked to depression are not obstructed to those with diabetes and may be related to the general emotional or mental distress of having a chronic disease [11].

The connection between depression and diabetes has been disputed to be essentially bi-directional (Fig. 1).

Brown *et al.* through a study have come to an end that depression increases the risk of diabetes rather than vice-versa [12]. Factors such as physiological and behavioral properties seem to play an important role in the relationship between depression and diabetes. Depression is conceivably related to impaired glucose tolerance and obesity [13]. And also, poor health behaviors such as smoking, physical inactivity, and caloric consumption found in depressed individuals may increase the risk of diabetes type 2 [14]. Depression is found to have association with mental or emotional abnormalities such as arousal of the hypothalamic-pituitary-adrenal axis, sympathoadrenal organization, and pro-inflammatory cytokines that will acquire an insulin resistance and contribute to diabetes risk [15].

Mezuk *et al.* conducted a study and reported a comparative risk of 1.62 for developing type 2 diabetes in patients with depression and a reliant risk of 1.21 for developing depression in diabetic patients [16].

ALTERED MENTAL STATUS BETWEEN PATIENTS WITH DM

Patients with DM seem not to be in higher risk for a mental disorder in general correlated to nondiabetic individuals.

Kruse *et al.* [17] did a cross-sectional population-based study of 141 diabetic patients, identified from a community sample of 4169 people, the prevalence of any mental disorder - assessed with the Composite International Diagnostic Interview (CIDI) - was commensurable between the patients having DM and the nondiabetic individuals (26.61% vs. 26.02%). After making changes for age limits, gender, socioeconomic status and family status, insignificant difference

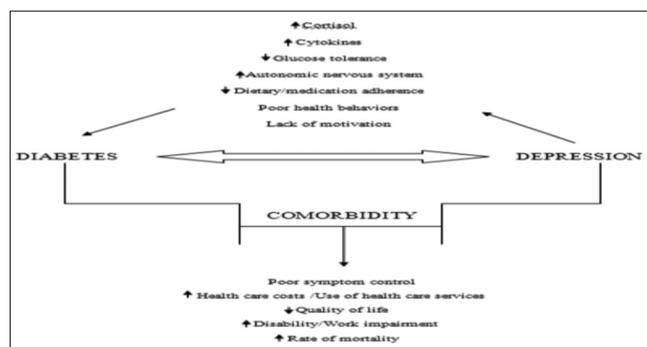


Fig. 1: Bidirectional relationship between comorbid depression and diabetes

between the two groups were found, only anxiety disorders were found to be significantly more prevalent in the diabetic group with OR=2.051; CI: 1.23-3.44.

Das-Munshi *et al.* [18] in another cross-sectional population-based study of 249 patients with diabetes, noticed out of a sample of 8580 individuals, the prevalence of any mental disorder - computed with the clinical interview schedule-revised was 21.62% in the diabetic group versus 16.32% in the nondiabetic group. The unadjusted odds ratio was nonsignificant (OR=1.4; CI: 1.01-2.02), but after adjustment of age, sex, and socioeconomic status emerged significant (OR=1.50; 1.11-2.20; $p < 0.05$). At the end, even after adjusting further for impairment in everyday functioning and medical comorbidity, the odds ratio was constricted again in nonsignificant levels. Same pattern was applied to mixed anxiety and depression, whereas the odds ratio regarding depressive, anxiety and comorbid anxiety-depressive disorders were not statistically meaningful throughout all the models applied, adapting for the confounders referred.

DEPRESSION

Prevalence and relative risk

The preponderance of major depression in patients with DM is mostly accounted around 12% (ranging from 8% to 18%), while temperate types of depression or elevated depressive symptoms, in general, are detected to be present in 16-35% (Table 1).

Compared to nondiabetic control community, patients with DM are reported to be about 1.3-3 times as expected to suffer from comorbid depression [18,26] although there have also been some studies - including the two fore mentioned [17,18] - that was unsuccessful to find out any genuine difference in the prevalence of depression (or affective disorders) between diabetic and nondiabetic individuals.

Pouwer *et al.* [19] suggested that the presence of comorbidities might be a significant factor contributing to the increased prevalence of depression in DM.

The concerning risk for the development of T2DM in depressed patients (depression→diabetes) is stated as high as 1.621. Conversely, pertaining to the relative risk for the development of depression in patients with DM (diabetes→depression), two recent meta-analyses of prospective studies have admitted a relative risk around 1.2 [16,35].

Estimates of the prevalence of depression change extensively depending on depression assessment tools (standardized interviews vs. self-report questionnaires), classifications of depression (discerning major from minor depression or referring to increased depressive symptoms), study designs (controlled vs. uncontrolled), sample sizes and diabetes type. Exactly, depression is found at a rate of about 2-3 times higher when in self-report questionnaires compared to major depression being assessed with standardized interviews [26,10].

Depressive symptoms seem to be marginally very much prevalent in T2DM compared to those with T1DM (Table 1 and 2). Further studies, which compare the prevalence of depression in samples containing patients with diabetes of either type, adjusting for potential confounders, such as age, diabetic complications, diabetes duration, treatment regimen, glycemic control, and medical comorbidity are needed.

PREVALENCES, ODDS RATIOS, AND RISKS CONCERNING COMORBID DEPRESSION IN DIABETES

Persistence of depression in diabetic patients

Persistence or recurrence has been stated to extend widely in review studies the rates of depression, between 11.67% and 92.13%, depending on sample sizes, principle of depression diagnosis and classification of depression (major depression or elevated depressive symptoms).

Lustman *et al.* [40] done a follow-up in 25 patients who had taken part earlier in a 8-week depression treatment clinical trial with nortriptyline versus placebo. Persistence of depression was assessed using the Diagnostic Interview Schedule and thus found out in 23 patients (92%), with an average of 4.8 depressive episodes over the 5-years of follow-up. Recurrence was so common (80% of the patients) and rapid (58.3% of the patients were depressed again within the first year) even after successful initial treatment of depression. At the time of review among the patients, major depression was found to be possible in 65.56% of the patients, and glycemic control was extremely worse in this group of patients when compared with those who are without depression. 19 patients (82.63%) those who relapsed had received extra courses of antidepressant treatment, but none was treated continuously for depression precaution.

A randomized controlled trial was conducted by Katon *et al.* [41] in 164 diabetic patients assigned to collaborative care intervention and then compared to 165 diabetic patients assigned to usual care, and he concluded that depressive symptoms - assessed with Hopkins Symptoms Checklist 90 (SCL-90) show that there is a persistence of depression in 59.90% of the intervention group when cross checked with 68.37% of the usual care group at the 12-month follow-up.

Fischer *et al.* [26] conducted a study among 508 patients with T2DM evaluated 3 times over 18 months with a baseline of 9 months and 18 months. Major depression was driven out with CIDI and found its presence in 14.9% of the patients at baseline and in 19.8% at any point during the study period. Major depression was persisted at all three estimated points in 11.6% of the patients diagnosed with major depression at baseline during diagnosis. Increased depressive symptoms were existing in 15.53% of the diabetic patients at baseline and in 34.42% at any point during the study. Increased depressive symptoms were prevailed at all three evaluation points in 58.12% of the patients with increased depressive symptoms at baseline. Thus, these findings indicated that prevalence of depression over time chiefly refers to increasing depressive symptoms rather than the major depression itself.

Katon *et al.*, [42] in a prospective study among 2759 diabetic patients who were followed up for 5 years and thus found that 83.01% of the patients with major depression founded for reporting ≥ 5 symptoms in Patient Health Questionnaire-9 (PHQ-9), including at least one core symptom of depression, such as depressed mood at follow-up had also been depressed at baseline, while 42.43% of them had also a positive experiences of depression based on the previous International classification of diseases (ICD-9) registry codes within a period of 18 months before the study.

Thus, we can conclude that depression is highly persistent and/or recurrent in DM, even after successful prior treatment. Thus, diabetic patients with a history of a depressive episode ever before should be deliberated at increased risk for reversion, especially under the influence of health-related or psychosocial stressors.

Table 1: Single studies (Cross-sectional design, point prevalences)

DM type	Sample	Depression assessment tool	Major depression	Minor depression	Reference	Year
Both	141 diabetics versus 4028 nondiabetics	1 CIDS 2 CIDI	10.2% versus 6.2% (refers to the prevalence of an affective disorder in general, including bipolar disorder)		Kruse <i>et al.</i> [17]	2003
T2DM	52 T2DM without comorbidity 162 T2DM with comorbidity 1184 healthy controls	CESD≥16	Overall T2DM (a+b) versus c: 9.3% versus 8.9%** 7.8% versus 8.9%, OR=0.94 (0.3-2.7) DM without comorbidity versus control: 7.8% versus 8.9%, OR=0.94 (0.3-2.7) DM with comorbidity versus control: 19.8% versus 8.9% OR=2.0 (1.1-3.5) 9.7% 12% T1DM versus without T2DM: 15.2% versus 10.7%; P<0.05 T2DM versus without T2DM: 19.0% versus 10.7%; P<0.001		Pouwer <i>et al.</i> [19]	2003
Both T2DM Both	1810 diabetics 4193 T2DM a. 223 T1DM b. 958 T2DM c. 59329 nondiabetic	CIDI-SF PHQ-9* HADS≥8			Egede <i>et al.</i> [20] Katon <i>et al.</i> [21] Engum <i>et al.</i> [22]	2003 2004 2005
Both	2266 T1DM, 371 T2DM, 35 unspecified type children and adolescents (10-22 years)	Major depression: CESD≥24 Minor depression: CESD: 16-23	8.6%		Lawrence <i>et al.</i> [23]	2006
Both Both Both	18,814 diabetics 249 diabetics versus 8331 nondiabetic Multiethnic study (WHO)	PHQ-8* CIS-R CIDI (major depression or dysthymia) CIDI (major depression or dysthymia)	7.5% (unadjusted) - 8.3% (age-adjusted) 14.7% versus 11.4% OR=1.4 (1.2-1.6)		Li <i>et al.</i> [24] Das-Munshi <i>et al.</i> [18] Lin <i>et al.</i> [25]	2006 2007 2008
T2DM	506 T2DM versus NCS-R sample	CIDI (major depression or dysthymia)	10.7% versus 6.7% 22.6%	1.6% versus 1.5%	Fischer <i>et al.</i> [26]	2008
Both Both	10,704 diabetics (beneficiaries) 16,754 diabetics	ICD-9 registry codes Major depression: PHQ-8 score≥10 Minor depression: PHQ-8 score: 5-9 CIDI (MD or dysthymia)	11.5% 14.7%		Katon <i>et al.</i> [27] Egede <i>et al.</i> [28]	2008 2009
Both	Random sample of 772 out of 2055 diabetics	CESD=16	Overall: 9%** T1DM: 7.8%; T2DM: 9.8% Overall: 32.9%** T1DM: 29.9%; T2DM: 36.3% 11.8%		Pouwer <i>et al.</i> , 2010.[29]	
T2DM	866 T2DM	Depression: DSQ score>7 Subthreshold depression: DSQ score: 5-7 Zung self-rating depression scale			Dirmaier <i>et al.</i> [30]	2010
T2DM	459 T2DM 232 NIT and 227 IT 417 T2DM		Overall: 14.1% Non-insulin treated: 14.7%; insulin-treated: 13.7%		Trento <i>et al.</i> [31]	2011
T2DM	260 subjects (130 with known T2DM and 130 controls without T2DM) 73 T2DM	PHQ-9 WHO-5 PHQ-9 PHQ-9	16.5% Overall 17.5% 46/130 (35.38%) versus 26/130 (20%)		Tapash roy <i>et al.</i> [32] Siddiqui <i>et al.</i> [33]	2012 2014
T2DM		PHQ-9	41% overall (4% severe, 10% moderate, 27% mild)		Thour <i>et al.</i> [34]	2016

1. CIDS: Composite international diagnostic screener, CIDI: Composite international diagnostic interview, CIS-R: Clinical interview Schedule-Revised, ICD: International classification of diseases, 2. CESD: Center for Epidemiological Studies - Depression, PHQ: Patient health questionnaire, HADS: Hospital anxiety and depression scale, DSQ: Depression screening questionnaire, NS: Nonsignificant, *Major depression: PHQ-9 or PHQ-8 symptoms≥5 with at least 1 important symptom (depressed mood or anhedonia) for≥7 days in the past 2 weeks; *Minor depression: PHQ-9 or PHQ-8 symptoms: 2-4 with at least 1 important symptom (depressed mood or anhedonia) for≥7 days in the past 2 weeks. **As calculated by the authors of this article. NIT: Non-insulin treated, IT: Insulin-treated

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Table 2: Systematic reviews and meta-analyses

DM type	Sample	Research design and methods	Major depression (MD)	Minor depression (MD)	Reference	Year
Both	20 studies (9 controlled) 11 studies did not contain comparison group	Systematic review	14.6%		Gavard <i>et al.</i> [36]	1993
T1DM and T2DM	42 studies (20 controlled)	Medline and psycINFO database Chi statistics and odds ratio	11.4%	Elevated depressive symptoms: 31% Controlled studies: 20.6% versus 11.3%; OR=2.0 Uncontrolled studies: 29.7% T1DM: OR=2.9 (1.6-5.5), T2DM: OR=2.9 (2.3-3.7) Overall: OR=2.0 (1.8-2.2) Not dependent of sex, DM type, sample source, depression assessment method	Anderson <i>et al.</i> [10]	2001
T1DM	144 adolescents	27 item self-report questionnaire	20% of youth with DM to <7% of youth without DM		Grey <i>et al.</i> [37]	2002
T1DM	4 controlled and 10 uncontrolled studies	Electronic databases and published references (January 2000-June 2004)	12% versus 3.2% (controlled studies) 13.4% (uncontrolled studies)		Barnard <i>et al.</i> [38]	2006
T2DM	10 controlled studies including a total of 51,331 people	Medline, embase and psycINFO database	17.6% versus 9.8% OR=1.6 (1.2-2)	The prevalence of depression was higher in females with DM (23.8%) compared with males (12.8%)	Ali <i>et al.</i> [39]	2006
T2DM	7 prospective studies	Medline	RR=1.15 (1.02-1.30)		Mezuk <i>et al.</i> [16]	2008
T2DM	11 prospective studies	Medline, embase and psycINFO database	RR=1.24 (1.09-1.40)		Nouwen <i>et al.</i> [35]	2010

T2DM: Type 2 diabetes mellitus, DM: Diabetes mellitus, OR: Odds ratio, RR: Relative risk

RISK FACTORS RESPONSIBLE FOR THE EVOLUTION OF DEPRESSION IN DIABETIC PATIENTS

Female sex, younger age, not having a partner, poor social support, lower education, low socioeconomic status, poor glycemic control, presence of diabetic complexities, presence of medical comorbidity, physical deterioration, and previous history of depression are the major risk factors associated with the presence of depression in patients with diabetes [20-22,42].

Pouwer *et al.*, [19] conducted a controlled community-based study in 216 patients with T2DM, observed from a sample of 3107 individuals (age range 55-85), and cross-checked the association of various factors with depression that are assessed both with CIDI and Center for Epidemiological Studies-Depression (CESD) scales using a 4-layer stepwise linear regression procedure, with demographics, clinical characteristics such as eye difficulties, CVD, other chronic medical diseases, medical comorbidity, functional limitations, social support, and perceived mastery over the disease were entered successively into the analysis. In the final model, they recognized the following risk factors being freely associated with depression. The female gender arose significantly associated with depression only in the first model. An association between depression and being unmarried arose as significant in the second and third model but ended up as marginally nonsignificant ($p=0.058$) again in the final model. Thus, indicated clinical characteristics were not significantly associated with depression in any of the stepwise regression models.

Egede and Ellis [28], in a large-scale cross-sectional study conducted among 16754 patients with DM, judged the differences among the three groups in which they created divisions in the sample by depression severity rating, according to PHQ-8 questionnaire scores. They found out indicative unsimilarities among the three groups by concerning race (four race groups), gender (females), age group (four classes), education status (four classes), assets (four classes), marital status (married), job status (employed), and allowance (insured), while no

significant differences were found concerning health provider and diabetes education. The differences found across the subgroups of the variables with more than two classes cannot be determined by the Chi-square analysis.

In a prospective study by Katon *et al.*, [42] the following risk factors for major depression were found out: A previous history of depression increased diabetes-related symptoms at baseline and cardiovascular procedures during the study. The presence of a history of depression is a significant factor that should be adjusted for a while evaluating risk factors associated with the development of depression in DM. The use of medication with a potential depressogenic effect is another factor that has not been sufficiently taken into accounts, such as certain antihypertensive agents for precedent that are often prescribed in patients with DM and comorbid hypertension.

SELF-CARE

Gonzalez *et al.* [43] in a meta-analysis of 43 studies came to a conclusion that depression was negatively associated with adherence to DM treatment regimen, based on almost all self-care aspects evaluated such as dietary intake, medication, exercise, self-monitoring of blood glucose level, medical appointment attendance and composite self-care measures, not including diabetic foot care.

Researcher's reports show that the type of diabetes did not seem to significantly affect the association between depression and nonadherence, and studies among children or adolescents with diabetes reported larger effects than studies among adults.

Gonzalez *et al.* [44] followed up 128 patients with DM for 9 months and concluded that, after modifying baseline self-care - assessed with diabetes self-care activities questionnaire, patients with higher depressive illness assessed with Harvard Department of Psychiatry showed lower attachment to general diet recommendations and specific dietary behaviors such as fruits and vegetables consumption

and spacing of carbohydrates, less physical activity, and poorer foot care at follow-up.

Katon *et al.* [45] in a prospective study among 4117 patients with diabetes, found that major depression announced as reporting ≥ 5 symptoms in PHQ-9 questionnaire, which includes at least 1 core evidence of depression, such as depressed mood or anhedonia was correlated with an increased likelihood of poor adherence to treatment concerning control of DM, hypertension and low-density lipoproteins.

Wagner *et al.* [46] conducted a study on 125 African American diabetic adults who were attending health fairs stated demographic and medical and medication history and provided blood samples for A1c assessment of glycemic control. He investigated the relationship between depressive symptoms and glycemic control, the relationship between depressive symptoms and long-term diabetes complications, the effects of demographic and diabetes variables on these relationships and the relationship between depressive symptoms and medication usage. Results show that higher depressive symptoms were related with elevated HbA1C, more long-term diabetes complications, and more diabetes medications. Diabetes self-care did not completely account for these relationships.

DIABETES-RELATED SYMPTOMS

Diabetes-related symptoms are more frequently stated in patients with comorbid depression.

Ciechanowski *et al.* [47] found that depression that is assessed with SCL-90R, as well as higher levels of diabetic complications, were independently affiliated with the amount of diabetes-associated symptoms reported for both T1DM and T2DM.

Ludman *et al.* [48] in a study among 4168 patients with DM, found that the symptoms associated with diabetes were assessed with self-completion patient outcome instrument was decidedly higher (mean = 4.40) in patients with major depression described by ≥ 5 symptoms in PHQ-9 scale, including at least one core sign or symptom of depression, such as depressed mood or anhedonia - against patients without depression (mean = 2.46).

McKellar *et al.*, [49] in a study among 307 patients with T2DM reviewed over 1 year and found that baseline depressive symptoms - evaluated with CESD and the mental health subscale of mental outcome studies 36-short form anticipated the diabetes-related symptoms which are categorized as hyperglycemic, hypoglycemic, and microvascular, changes over the follow-up period. However, when self-care cohesion was entered in the structural equation model, the relationship between depressive and diabetes-related symptoms stayed no longer significant which indicates that the negative collision of depressive symptoms on diabetes-related symptoms is indirect, probably mediated by the negative collision of depression on diabetes self-care.

DIABETIC COMPLICATIONS

A meaningful association between depression and diabetic complications has been recognized.

According to a meta-analysis by de Groot *et al.*, [50] the effect sizes for each complexity were as given as: 0.17 for retinopathy, 0.20 for macrovascular complexities, 0.25 for neuropathy, 0.28 for neuropathy, and 0.32 for sexual dysfunction. The overall effect size was small to moderate ($r=0.25$), commensurable between the two types of diabetes. The majority of studies on the relation between depression and diabetic complications have been cross-sectional, thus making causality difficult to conclude. However, prospective studies have presented that depression is associated with a higher and more rapid incidence of diabetic complications (Table 3).

Black *et al.* [55] studied combined effects of depression and diabetes on the incidence of adverse health outcomes among 2,830 Mexican

Americans aged ≥ 65 years. Longitudinal data from the EPESE survey were used to examine the main effects and interaction effects of diabetes and depressive symptoms he found synergetic interaction of diabetes and depression, predicting greater mortality, greater occurrence of both macro- and microvascular complications, and greater incidence of restriction in activities of daily life, even when controlling for sociodemographic characteristics such as gender, age, educational status, and marital status.

A study conducted by Thour *et al.*, [34] assessed the prevalence of comorbidities in 73 subjects. The mean age of study population was 50.8 ± 9.2 years. 57.5% of the subjects were females. 38.4% were from rural area. 60% of them had coexistent hypertension. About 40% had at least one microvascular complications.

The associations between depression and diabetic complications appear to be bi-directional, since depression might be a result with poor glycemic control as an intermediary - in advanced course of complications on one hand, while on the other hand, complexities might also have a contradictory impact on patient's physical and mental health and QOL, thus promoting the development of depression.

COGNITIVE IMPAIRMENT

According to a systematic review of prospective studies by Cukierman *et al.* [56] People with diabetes have been reported to be at 60% increased the risk of developing dementia.

Mixed results were produced from studies evaluating the impact of depression on cognitive impairment in patients with DM.

Bruce *et al.* [57] assessed the longitudinal predictors of dementia in a study conducted between 302 patients with DM. Dementia after review was found not significantly associated either with depression at check out (cross-sectional) or with depression at baseline (longitudinal).

Katon *et al.*, [58] in a prospective cohort study of 3837 primary care diabetic patients, over a 5-year follow-up period, evaluated the impact of depression on the risk for developing dementia. They found a significantly increased incidence of dementia (21.52 per 1000 person) in DM patients and major depression at baseline distinguished with DM patients but no depression at baseline (incidence rate of 11.81 per 1000 person). Thus, comorbid major depression in DM was prospectively associated with a three-fold increased probability of dementia.

Katon *et al.* [59] governed a prospective cohort study in 3,837 primary care patients with diabetes (mean age 63.2 ± 13.2 years) registered in an HMO in Washington State. Depression at baseline was determined using the PHQ-9, and ICD-9 diagnoses for dementia were used to identify cases of dementia. Over the 5-year period, 36 of 455 (7.9%) patients with major depression and diabetes (occurrence rate of 21.5 per 1,000 person-years) versus 163 of 3,382 (4.8%) patients with diabetes alone (occurrence rate of 11.8 per 1,000 person-years) had one or more ICD-9 diagnoses of dementia. Thus, he concluded that patients with comorbid major depression had an increased exposure of dementia (fully adjusted hazard ratio 2.69, 95% CI: 1.77, 4.07).

ASSOCIATION OF OBESITY

Mellal *et al.* [60] in a study about the prevalence of depressive symptoms and its socioeconomic determinants among university students in Al Ain, UAE found that the prevalence of depression was 22.2% among the study sample. Age seems to be associated with a significant difference in the prevalence of depression with the highest rate in the age group 17-25. Students those who asserted facing financial problems had a significant higher prevalence of depression. Finally, students' ideas to their weight were associated with a significant influence on the prevalence of depression. Those who demanded being overweight had a significant higher prevalence of depression.

Table 3: Depression and diabetic complications risk

Reference	Year	Sample size	Complication	Follow-up time	Depression rate	Method
Roy <i>et al.</i> [51]	2007	483 African American patients	1. Retinopathy 2. Proliferative retinopathy	6 years	OR=2.44 (1.01-5.88; P=0.04) OR=3.19 (1.30-7.87)	Administration of BDI, a detailed ophthalmologic examination, retinal photographs and measurement of HbA1c as an index of glycemic control
Lin <i>et al.</i> [52]	2010	4623 primary care patients with T2DM	1. Advanced microvascular complications (blindness, ESRD, amputations, and renal failure death) 2. Advanced macrovascular complications (MI, stroke, cardiovascular procedures and death)	Enrolled in 2000-2002 and followed through 2005-2007	HR=1.36 (1.05-1.75) HR=1.25 (1.0-1.54)	Medical recorded review, ICD-9 diagnostic and procedural codes and death certificate data were used
Clouse <i>et al.</i> [53]	2003	76 female patients	1. CVD 2. Cerebrovascular	10 years	HR age-adjusted=5.2 (1.4-8.9) Non-significant	A multivariate model incorporating other CHD risk factors such as age, duration of DM, BMI, HbA1c, presence of hypertension and hyperlipidemia or tobacco use were used
Williams <i>et al.</i> [54]	2011	1289 major 2541 minor	Amputation	4.1 years	1. Major: HR=1.33 (1.15-1.55) 2. Minor: HR=1.01 (0.90-1.13)	Details about 531973 veterans from the diabetes epidemiology cohorts, a National VA registry and Medicare data were collected

BDI: Beck depression inventory, VA: Veterans affairs, DM: Diabetes mellitus, T2DM: Type 2 diabetes mellitus, CVD: Cardiovascular disease, HR: Hazard ratio, OR: Odds ratio, MI: Myocardial infarction, ESRD: End stage renal disease

Arafat *et al.* [61] in a study *about* the association of type 2 diabetes with obesity and other factors: In multinational community found a significant difference between the presences of type 2 diabetes in obese volunteers when compared to that of nonobese volunteers regardless of their age, race, and gender. However, the study showed that gender, age, race, family history with type 2 diabetes, and quality of food taken as one of the contributed factors that can induce type 2 diabetes, even in the nonobese adults.

CONCLUSION

Depression is common in both types 1 and 2 diabetes and has a significant role on the course and outcome of this medical illness. In a primary care population, diabetes self-care was suboptimal across a continuation from home-based activities, such as healthy eating, workout, and medication adherence, to use of preventive care. Major depression was chiefly associated with patient-initiated behaviors that are not easy to support (e.g., exercise, diet, and medication adherence) but not with preventive services for diabetes. Depression is a matter of great concern in patients with DM. It is not only highly accepted, but also highly persistent and recurrent causing a significant negative impact on both clinical outcomes and QOL. Besides, impaired QOL, it further deteriorates clinical outcomes and has been prospective leads to increased mortality in DM. Frequency of primary care visits (≥ 7), female gender, poor self-rated physical health, panic attacks, and dysthymia were agents independently associated with increased probability for correct depression recognition. Coming to the management of depression in DM, psychotherapy combined with psychoeducational

interventions or collaborative care seem to be cost-effective and yield beneficial and good results, both on mental health outcomes as well as diabetes management and glycemic control.

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