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Review

# Depression in type 2 diabetes mellitus—A brief review

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ABSTRACT

Diabetes mellitus is a chronic disease which has been associated with depression. Depression is more common in adults with type 2 diabetes mellitus (T2DM) as compared to those without. Both micro- and macro vascular diabetic complications are associated with depression and have shown to increase the risk of mood disorder. Further, poor glycemic control in T2DM patients could lead to more complications of diabetes and such patients are more likely to develop depression. More research is needed in this area to determine the exact relationship between depression and T2DM and to unfold the mystery of mechanism behind this.



**Contents**



## 1. Introduction

Diabetes mellitus is a group of metabolic diseases that leads to a substantial reduction in life expectancy, decreased quality of life, and increased costs of care. The global prevalence of type 2 diabetes mellitus (T2DM) has been estimated to be 6.4% [1]. The World Health Organization has projected that around 300 million people will suffer from diabetes by 2025 [2]. T2DM is much more prevalent as compared to type 1 diabetes. It comprises 90% of people with diabetes around the world [3], and is caused by a combination of resistance to insulin action and an inadequate compensatory insulin secretory response [4].

Depression is a common co-morbid condition in T2DM and it has been estimated that people with T2DM are twice as likely as the general population to suffer from depression [5,6].

Individuals with diabetes and co-morbid depression have been shown to have poor adherence to diabetes medications [7], poor adherence to dietary recommendations [7], poor glycemic control [8], more diabetes-related complications [9], and a higher risk of mortality than individuals with diabetes who are not depressed [10,11]. American Diabetes Association (ADA) has also recommended the assessment of psychological problems like depression in the patients with diabetes [12].

## 2. Depression and type 2 diabetes

A relation between depression and T2DM has been indicated in several clinical reports [5,13,14]. However the direction of the relationship is unclear. For example the research by Knol et al. suggests that depression being a consequence of diabetes may also be a risk factor for the onset of diabetes [15]. Individuals with depression, but no diabetes, are at a higher risk for developing diabetes at follow-up. Mezuk et al. reported data showing that depression may be an important risk factor for developing T2DM. Depression was associated with a 60% increased risk of developing T2DM [16]. The reason for this could be that people with elevated depressive symptoms are less attentive toward a healthy lifestyle, therefore increasing their risk for diabetes. Conversely, individuals with no depression, but receive diabetes treatment, are at a higher risk for developing depression at follow-up [17]. A recent

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meta-analysis has reported 24% increased risk of incident depression in T2DM patients as compared with non-diabetics [18]. These findings among others [13,19] suggest that there is strong evidence for a bidirectional relationship between diabetes and depression. Golden et al. also found evidence for a bidirectional relationship within the same cohort [14].

Literature reports that patients with diabetes are almost twice as likely to suffer from depression as the general population [20,21], with women at a higher risk with prevalence of 28.2% compared to 18% among males [5,6,22–24]. Several other studies have reported the prevalence rates of depression in T2DM patients between 24 and 30% [5,6,25].

However, recently it has been suggested that although up to 30% of individuals with diabetes report depressive symptoms, only about 10% have major depression [26]. A fact which cannot be ignored is that the published studies differ widely in terms of the methods used to measure depression, which makes any conclusions premature. Rates of depressive symptoms have been found to be higher in those studies where self-report instruments were used compared to diagnostic interviews [5].

Several neuroendocrine and neurotransmitter abnormalities common to both depression and diabetes have been identified which, to some extent can explain the close relationship between these two. One of the findings refer to chronic dysregulations of the hypothalamic–pituitary–adrenal (HPA) axis such as high cortisol levels and reduced insulin sensitivity or an activation of the immune system leading to or fostering chronic inflammatory processes [27].

The risk factors for depression in the patients with T2DM include comorbidity of diabetes-related complications, in particular vascular complications [28,29]. Knowledge of having diabetes [14], longer duration of diabetes [30,31], more demanding regimens, low levels of daily activities [32], smoking [33] and obesity [34,30] have all been postulated as risk factors, but the epidemiological evidence remains limited.

Other studies have suggested that an increased level of depression is associated with demographic variables such as low education [6], female sex [13,30,35], or being unmarried [6].

Potential risk factors for depression in people with diabetes often interact with each other and with other factors. For example, the relationship between duration of diabetes and depression may be confounded by the number of complications present.

It has been reported that duration of diabetes is associated with the development of depression. Increased duration of the disease is known to significantly increase the risk for developing diabetic complications and health care expenditures, as a result such patients are more prone to develop psychological illnesses [36].

Depression in T2DM has been found to be associated with diminished quality of life [37] and poorer diabetes self-care [38]. A recently published World Health Organization (WHO) World Health Survey about the impact of depression on quality of life in different chronic diseases (arthritis, asthma, angina and diabetes) showed that quality of life was most impaired in patients with diabetes and depression [39]. For women with type 2 diabetes, negative moods have been reported to impact their day-to-day living and overall quality of life [40]. And they have been reported to have poorer glycemic control and quality of life than men with diabetes [41]. Depression in T2DM decreases compliance with medications and healthy lifestyle measures, increase health care expenditures, and above all increase the risk of cardiovascular mortality [42].

## 3. Pathophysiology of depression and type 2 diabetes-linked

The reason for this timely relationship between depression and diabetes manifestation is unclear. It could be that people with elevated depressive symptoms are less attentive toward a healthy lifestyle, therefore increasing their risk for type 2 diabetes. Alternative explanations for this finding refer to chronic dysregulations of the hypothalamic–pituitary–adrenal (HPA) axis such as high cortisol levels and reduced insulin sensitivity or an activation of the immune system leading to or fostering chronic inflammatory processes [27] (see Fig. 1). A second explanation for the close relationship between depression and diabetes comes from the observation that depressed patients with diabetes also report a high amount of diabetes-related distress [43]. It might be that in vulnerable patients a high amount of diabetes-related distress or a deficit in coping with diabetes-related problems could result in elevated depression symptoms. A third explanation stems from study results indicating that blood glucose is itself a potent regulator for mood states. In particular, hypoglycemia or severe hyperglycemia is able to induce negative emotional states in patients with diabetes [44].

## 4. Depression and diabetic complications

Poorly controlled diabetes leads to a number of co-morbid complications. These include diabetic retinopathy, nephropathy, neuropathy, cardiac heart diseases and peripheral vascular disease. Association between depression and various long-term diabetic complications have been reported in several studies [43,45,46]. The prevalence of depression in T2DM patients appears to increase with the number of diabetic complications [47]. Two recent reviews have reported that depressed mood is positively associated with the presence of diabetic complications and it has been investigated that the prevalence of depression is higher among T2DM subjects with retinopathy, neuropathy, nephropathy and peripheral vascular disease (PVD) [28,48].

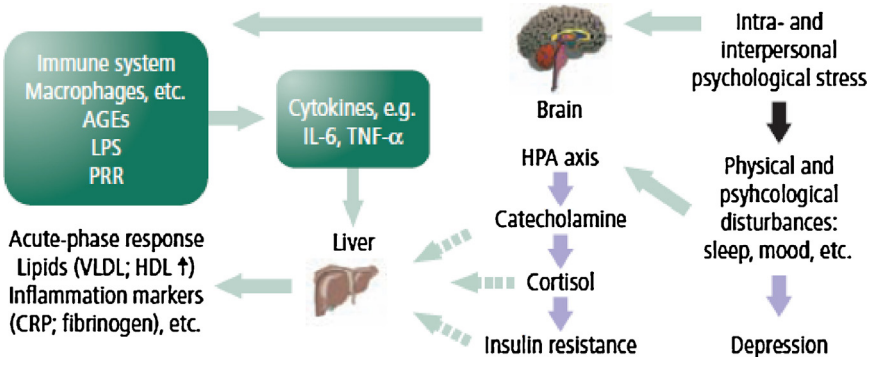


**Fig. 1.** Possible pathophysiological pathways linking depression and diabetes.