

A causal relationship between diabetes mellitus and depression

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Abstract

In today's modern world depression has become a common stress factor among both men and women irrespective of age. But to be specific, it has been found that there is a strong relationship between diabetes and depression. The rate of this relationship seems to be higher and much literature suggests us the numbers could be increasing in the future. Depression in diabetes may arise due to some factors such as comorbidities, improper management of blood glucose level, patient's financial status in managing the conditions can precipitate depression. Other physiological factors like the increased sympathetic nervous system, HPA-axis, and increased cortisol in the brain can contribute to the development of diabetes and depression. This comorbid condition of depression and diabetes decreases the quality of life. On the other hand, people with depression have a high incidence of developing diabetes. Depression has been a significant risk factor in developing diabetes, especially T2DM. Several neuroendocrine and neurotransmitter disorders are found along with depression and diabetes this closely relates and explains the relationship between the two conditions. Insulin resistance a specific risk factor was found to correlate depression and diabetes. Antidiabetic drug, thiazolidinedione was found to lessen the effect of both depressive disorder and insulin resistance in individuals experiencing diabetes and depression.

Keywords: Depression; Diabetes mellitus; Relationship

1. Introduction

Both diabetes and depression are prevalent illnesses in today's culture. The American Diabetes Association (ADA) also advised that diabetic people be evaluated for psychological issues like depression [10]. Approximately 200 million people worldwide today have diabetes. By the year 2025, the number will approach 333 million if nothing is done to stop the disease [1]. Additionally, it is believed that 121 million individuals worldwide experience depression today. In any given year, 6% of men and 10% of women will have a depressive episode [2]. By 2030, it is anticipated that both conditions will rank among the top five primary causes of disease burden [3]. Both diabetes and depression are linked to morbidity and mortality, and when these two conditions coexist, there is an increased chance of acquiring comorbidities, ineffective blood glucose management, complications, and complaints, as well as higher medical costs [8,9]. Since then, numerous longitudinal studies have looked into the link between depression and the onset of type 2 diabetes, with varying degrees of success [4]. Some claim that several longitudinal prospective population-based studies have recently focused on the temporal link between depression and diabetes. Depression was linked to an elevated incidence of incident diabetes in three systematic reviews and meta-analyses. One prior systematic review and meta-analysis that focused on the opposite, that diabetes may be a risk factor for depression, included seven research. Other studies do not reveal a significant correlation between depression and type 2 diabetes. Depression is related to an increased risk of developing type 2 diabetes [5,6]. According to Thomas Willis, a renowned anatomist and member of

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the Royal Society who founded the organization, "diabetes is a consequence of prolonged sorrow" in the 17th century [11]. The most prevalent psychological condition, depression, is more prevalent in diabetic patients than in the general population [7]. While one in four adults with type 1 and type 2 diabetes experience significant depression symptoms, only 10% to 15% of diabetics formally diagnose a depressive condition [12].

2. Depression and diabetes mellitus

Willis noted in the late 17th century that persons who suffered "significant life stress, sadness or long sorrow" were more prone to diabetes. This relationship between depression and diabetes has already been established for a long time [15]. People who have depression but no diabetes are more likely to develop diabetes over time. According to findings published by Mezuk et al., depression may be a significant risk factor for developing T2DM. T2DM risk was 60% higher in individuals who had depression [12]. Individuals who are treated for diabetes who do not now have depression run an increased chance of developing it in the future [13]. Due to the disease's immediate and long-term problems, daily insulin injections, routine blood glucose monitoring, physical complications, hospitalization, and diabetes-related restrictions, diabetic individuals are vulnerable to psychiatric illnesses [14]. Diabetes and depression have several neuroendocrine and neurotransmitter disorders, which in part explains why these two conditions are closely related. One of the findings is related to long-term dysregulations of the hypothalamic-pituitary-adrenal (HPA) axis, including elevated cortisol levels, decreased insulin sensitivity, or immune system activation that causes or promotes chronic inflammatory processes [16]. Patients with T2DM who also have concomitant diabetes-related comorbidities, particularly vascular problems, are at increased risk for developing depression. The epidemiological evidence is still sparse, however, risk variables such as knowledge of diabetes, longer diabetes duration, more demanding regimens, low levels of daily activity, smoking, and obesity have all been proposed [17]. It has been discovered that depression in T2DM is linked to worse quality of life [18] and worse diabetic self-care [19]. Depression in T2DM reduces adherence to prescription drugs and healthy lifestyle practices, raises healthcare costs, and, most importantly, raises the risk of cardiovascular mortality [20]. Negative emotions have been shown to impact daily life and overall quality of life for women with type 2 diabetes [21]. Additionally, they are said to have lower glycemic control and a lower quality of life than diabetic men [22].

3. Pathogenesis of diabetes mellitus and in association with depression:

The co-morbidity of diabetes and depression has been the subject of numerous studies over the past ten years because of the detrimental effects on both individual health and the healthcare system. In 2015, three possible routes for the relationship between diabetes and depression were suggested by two separate reviews: both diseases may have the same etiology; diabetes increases the prevalence or risk for future depression; and depression increases the prevalence or risk for future diabetes [23]. The positive correlation between depression and type 2 diabetes cannot be linked to any shared genetic markers, according to recent studies [24]. However, several environmental factors may open up shared pathways that, in the end, encourage DM2 and depression. The low socioeconomic level is a significant factor that raises the risk of DM2 [25] and may also contribute to depression [26]. Chronic stress is one of the factors that activate the sympathetic nervous system (SNS), the hypothalamus-pituitary-adrenal axis (HPA-axis), and the adrenal medulla, boosting the synthesis of cortisol in the adrenal cortex and of adrenalin and noradrenaline in the adrenal medulla [27]. Chronic stress has behavioral repercussions. Noradrenaline, cortisol, and other hormones activate the fear system, determining whether a person will have anxiety, anorexia, or hyperphagia. The same mediators also trigger tachyphylaxis of the reward system, which results in sadness and desires for food, other substances, or stress [28]. Additionally, ongoing stress increases the production of inflammatory cytokines either directly or indirectly via the HPA axis or SNS. High levels of inflammatory cytokines interfere with the pancreatic β -cells' ability to function normally, cause insulin resistance, and hence encourage the development of DM2 [29,30]. When compared to youth without diabetes, young people with diabetes have a two- to three-fold higher prevalence of depression [31]. Contrary to what was previously believed, it appears that DM1 and depression share similar pathophysiological routes to DM2 and that the burden of diabetes increases the prevalence of depression [32].

4. Diabetes a risk factor for depression:

Having biological relatives who have depression, traumatic childhood events, stressful life events, alcohol and drug abuse, and having a significant somatic ailment are all considered standard risk factors for depression. According to the results of meta-analyses, there may be a bidirectional relationship between depression and type 2 diabetes. This means that, in addition to depression's ability to predict the onset of the disease, type 2 diabetes may also have a small but significant predictive power for depression [33,34]. This finding emphasizes the significance of taking diabetes and prediabetes into account as risk factors for depression, together with the fact that indications of prediabetes (such the

metabolic syndrome) might predict the onset of depression [35]. Results of a meta-analysis of cross-sectional population-based research published up to 2011 indicate that there may be a tenuous positive relationship between adult depression symptoms and insulin resistance. The researchers did note a significant amount of variation amongst studies, with some showing significantly greater correlations with measures of depression (interview-based or treated depression) and insulin resistance (non-fasting estimates) that were more exact [36]. However, given participants in some of the studies included in this meta-analysis had diabetes (and were thus insulin-resistant by diagnosis), it's possible that the sporadic positive link is driven by the association between overt diabetes and depressed symptoms. Additionally, despite significant heterogeneity in both variables, a relationship between insulin resistance and depression was not identified in one research within the usual range of glucose tolerance [37]. According to research, thiazolidinediones, a class of anti-diabetic medications, may lessen insulin resistance as well as depressive symptoms in diabetics who also have severe depressive disorder [38]. Similar improvements in insulin resistance were documented in research comparing the effects of pioglitazone and metformin, another medication that increases insulin sensitivity, however, patients in the metformin group did not see a decrease in depressive symptoms [38]. Self-care practices, complications, and the ensuing physical limits may raise the likelihood of depression or depressed symptoms in more advanced stages of diabetes. Complex self-management techniques, worry about therapy, and difficulty coping may all contribute to an increase in depression symptoms among diabetics [39]. Therefore, the stress of managing diabetic complications and concomitant conditions (particularly cardiovascular disease) may result in depressive symptoms [40,41].

5. Depression and diabetes complications:

Diabetes that is not well-controlled can cause a variety of co-morbid problems. These include peripheral vascular disease, nephropathy, diabetic retinopathy, and neuropathy. Numerous studies have found a connection between depression and other long-term diabetes problems [42,43,44]. It has been observed that the incidence of depression is positively correlated with the existence of diabetes complications, according to two recent reviews, and greater among those with type 2 diabetes who also have peripheral vascular disease (PVD), retinopathy, neuropathy, and nephropathy [45]. According to Yoshida et al.'s research, depression is linked to microvascular complications, specifically neuropathy, regardless of age, gender, marital status, social support, pain perception, perception of general health, type of diabetes, duration of diabetes, glycated hemoglobin levels, and insulin requirement [46]. On the other hand, functional impairment in people with T2DM has been linked to a higher frequency of depression. The underlying processes that account for this relationship, however, remain to be elucidated [47]. Effect sizes ranged from 0.17 to 0.32 and were mild to moderate. The development and prevalence of coronary heart disease, according to Clouse et al., affected diabetic women who had depression [48]. Additionally, studies have revealed a link between depression, poor glycemic control, and diabetes complications in racial and ethnic minorities [49]. Depressed people with diabetes in an American Indian community in Arizona (USA) also had worse glycemic control [50]. According to a meta-analysis, diabetics with co-morbid depression are 38 and 33% more likely than controls without depression to experience macrovascular and microvascular problems, respectively [51].

6. Clinical consequences of comorbid depression and diabetes:

Comorbid gloom antagonistically influences diabetes results and diminishes personal satisfaction [52,53,54]. A postal review of 4168 individuals with diabetes saw that as contrasted and those without sadness, the 487 individuals with significant sorrow detailed fundamentally more diabetes side effects and the number of burdensome side effects connected with the general number of diabetes side effects [55]. Different studies of the relationship between depression and adult glycemic control have found conflicting results. Some show that depression is associated with a small decrease in glycated hemoglobin, while others show that depression has no effect [56,57,58]. Depressive symptoms are more clearly linked to poorer glycemic control in children and adolescents [59]. By the by, discouragement is related to demolished seriousness across the full scope of diabetes intricacies albeit the bearing and components that underlie this affiliation are not completely perceived [60]. Sorrow, regardless of whether gentle, is likewise connected with untimely mortality through a scope of states of being [61]. In the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial, clinically significant depressive scores were an independent risk factor for all-cause mortality after adjustment for blood pressure, glycated hemoglobin, lipids, body mass index, aspirin use, tobacco, alcohol, living alone, and educational level. As a result, the excess mortality cannot be entirely explained by an increase in known risk factors [62].

7. Conclusion

Depressive disorders are becoming a serious risk factor among diabetic patients. As this condition is emerging slowly. The majority of the cases were found to have depressive disorders due to their improper management in treating diabetes and patient-specific status in managing the condition. This article emphasized some common factors that cause depression in diabetes and the relationship between them. Management of depressive disorders has to be closely monitored and strategies have to be developed in treating depressive disorders in diabetic patients.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest is to be disclosed.

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