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Review

Exploring the Interrelationships Between Diabetes, Nutrition, Anxiety, and Depression: Implications for Treatment and Prevention Strategies

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Abstract: Diabetes and mental disorders have been recognized as two significant public health concerns globally. Recent research indicates that there is a bidirectional relationship between these two conditions, with each influencing the other's course and outcomes. Nutrition plays an essential role in the prevention and treatment of both mental disorders and diabetes. A comprehensive review of existing literature was conducted to examine the impact of anxiety and depression on the development of diabetes and the influence of diabetes on the occurrence of mental health disorders such as anxiety and depression. Additionally, the effects of nutrition on the prevention and management of mental disorders, diabetes, and related complications in at risk individuals were assessed. Our findings show that mental disorders, such as depression and anxiety increase the risk of developing type 2 diabetes and are associated with poorer glycemic control, increased diabetes-related complications, and higher mortality rates. Conversely, diabetes is also linked with an increased risk of developing mental health disorders, including depression, anxiety, and cognitive decline. The biological, psychological, and social factors that contribute to the comorbidity between these two conditions are complex and multifaceted. Therefore, an integrated approach to the management of both conditions is critical for improving patient outcomes and reducing the overall burden of disease. Nutritional interventions should be utilized to reduce the risk of diabetes in patients with anxiety and depression as well as enhance mental health in patients with diabetes.

Keywords: diabetes; mental health; anxiety; depression; supplementation; nutrition; blood glucose; cardiovascular health; cognitive decline; mental disorders; nutrition education.

1. Introduction

According to the International Diabetes Federation, diabetes has been noted as one of the most devastating diseases in the 21st century while many people remain undiagnosed [1]. Meanwhile, one in three adults has prediabetes [2]. The occurrence of diabetes is troubling as studies uncovered 463 million patients with diabetes in 2019, and the prevalence will potentially increase to 578 million by 2030 [3]. The incidence is expected to increase further, with estimates of more than 600 million people affected by 2040 [1]. As with most chronic diseases, many factors contribute to the occurrence and treatment of diabetes, including mental health.

Anxiety and depression have become widespread mental disorders identified by cognition, mood, and attitude variations that significantly impact an individual's well-being and daily life [4,5]. Depression disorders have been estimated at approximately 17%, while the prevalence of anxiety disorders is about 29% [5–7]. Considerable evidence confirms that mental health disorders enhance appetite and cravings and decrease motivation for physical activity [8]. Furthermore, high sugar intake has been associated with depression and anxiety in numerous cross-sectional and observational studies [9–12]. Along the same lines, research studies have identified a link between the intake of refined carbohydrates and circulating inflammatory markers and their impact on mental health [13,14]. It has been reported that patients with mental disorders have a reduced intake of vegetables, fruits, whole grains, and fiber in their diet [15,16]. As a result, a low-quality diet consumed

during episodes of depressive symptoms may elevate the risk of diabetes. Depression can also contribute to an increased risk of diabetes through biological mechanisms, particularly by impacting hormonal regulation associated with mood disorders. [17]. Such processes include increased proinflammatory cytokines and abnormalities of the hypothalamic-pituitary axis (HPA) [18]. Cortisol, one of the HPA axes hormones, is known to increase appetite and ramp up motivation for the intake of calorically dense foods which may increase blood glucose levels in at-risk populations [19,20].

Although anxiety and depression could be risk factors for diabetes, there is also an inverse effect of diabetes on mental health. Generally, individuals with poor glycemic status have a greater chance of developing anxiety and depression [2,17]. It has been shown that prevalence rate of depression in individuals with prediabetes is three times and in patients with diabetes is two times higher than the general population [7]. Impaired glucose metabolism, management of symptoms, diminished response to treatment, and the fear of developing other complications could put patients with diabetes at higher risk of developing mental disorders and lower quality of life [21]. In adults with diabetes, 18% have been reported to require psychiatric support; however, it is reported that 10% of these mental health conditions go undetected [22]. The duration of diabetes and glycemic control are significant determinants contributing to mental disorders in adults diagnosed with diabetes [23]. Nutrition intervention offers a potential avenue for preventing or mitigating symptoms of mental health conditions and diabetes. The primary objective of this literature review was to examine the interplay between mental health and diabetes and investigate the role of nutrition in preventing or managing these interconnected conditions.

2. Materials and Methods

To gain insights into the relationship between depression, anxiety, and diabetes, a comprehensive literature review was undertaken to examine the existing evidence concerning the influence of depression and anxiety on the onset and management of diabetes, as well as the impact of diabetes on the occurrence and severity of symptoms in depression and anxiety disorders. The inclusion criteria for this study included observational studies, clinical trials, systematic reviews, and meta-analyses sourced from reputable databases, including PubMed, Google Scholar, and George Mason University Library. The search covered the period from 2000 to 2023. In addition, these keywords and phrases were used to increase the effectiveness of searches within the databases: "diabetes," or "depression" or "anxiety" or "mental health" or "risk factors" or "symptoms" or "mechanisms" or "Nutrition". We finally searched for all peer-reviewed studies on the topic to ensure all relevant articles were included.

3. Results

Research has demonstrated a causal relationship between mental health and diabetes. It has been shown that depression and anxiety are more prevalent among individuals with diabetes compared to healthy populations (26.3% vs. 11.2%, respectively) [24]. On the other hand, it has been suggested that individuals with established mental health disorders are at increased risk of developing diabetes later in life [25]. A systematic review done in 2021 looked at the association of psychiatric disorders with diabetes risk and found a relative risk of 1.60 for individuals with depression and an odds ratio of 1.47 for individuals with anxiety disorders [26].

3.1. Investigating the Effects of Diabetes on Depression Risk

Diabetes is associated with the onset and worsening of depression and overall depressive symptoms [27]. The occurrence of depression is two to three times higher in individuals with diabetes compared to individuals with normal blood glucose [28]. Approximately one in four adults with diabetes have depression while only 25% to 50% of them get diagnosed and treated [29]. Treatment regimens for individuals with diabetes include the use of multiple medications, blood glucose monitoring, adherence to specific dietary guidelines, and attending regular medical check-ups [25].

These treatment approaches are aligned with the challenges faced by individuals dealing with diabetes or its associated complications. Patients with diabetes may experience depressed mood, weight loss or gain, sleep disturbances, fatigue, stress, and decreased libido which can have a dramatic effect on their mental health [30]. The relationship between living with diabetes and treating diabetes can give way to a foundation for the development of depression [30]. For patients with diabetes, even with high-quality treatment that could help to lessen the strain of diabetes, several factors still play a role in increasing the risk of depression; factors such as the psychological burden of being ill, unfavorable lifestyle, physician ignorance, or alterations in the activity of the hypothalamus–pituitary–adrenal axis (HPA) axis [31–33]. The HPA axis is an area of the brain that controls reactions to stress as well as regulates various body processes [7]. The interactions between the hypothalamus, pituitary gland, and adrenal glands can cause alterations to cortisol production, which could be an underlying mechanism of increased depression risk in people with diabetes [33,34].

The diagnosis of diabetes can be overwhelming for some people given the association it has with debilitating complications. In a study done by the European Depression in Diabetes (EDID) Research Consortium, patients diagnosed with diabetes were found to have higher incidences of depression suggesting that the knowledge of the diagnosis and the burden of treating the condition and its complications are associated with depressive symptoms [35]. This makes the case for doctors and healthcare providers to increase their role in the psychological aspects of their patient's diagnosis. Another element contributing to depression is lifestyle factors such as sedentary behaviors and diets high in saturated fats and refined sugars, which may assist in priming or reinforcing the comorbidity of depression [35]. Additionally, it has been shown that poor glycemic control and greater glycemic variability are associated with reduced quality of life and negative moods [21]. This raises the possibility that there may be a mutually reinforcing phenomenon in which reduced self-care compliance increases blood glucose levels, which may contribute to depressive symptoms [35,36].

Controlling diabetes and depression together requires a multifaceted approach. Compared to those without depression, these individuals typically have higher glycemic levels, use health services more frequently, and have higher rates of complications [30]. A primary care study of 879 people with type 2 diabetes (T2DM) revealed that nonadherence to self-care management was causally related to hyperglycemia and diabetes complications [37]. Furthermore, individuals with diabetes and depression have been linked to a higher mortality rate [38].

3.2. Examining the Impact of Depression on Diabetes Risk

Not only does diabetes increase the risk of depression but also individuals with depression might be at higher risk of diabetes. Depression is a major psychiatric illness that impairs the quality of life and puts enormous burdens on the healthcare system [39]. The behavioral, biological, and cognitive mechanisms associated with depression have been shown to increase the risk of diabetes development [40]. Health issues within these mechanisms seem to work in a continuous loop where they are in response to depression and a reason for the development of diabetes. Issues related to depression such as unhealthy eating habits, physical inactivity, or sleeping disturbances (behavioral) contribute to weight gain, increased activity in the HPA axis, and increased insulin resistance (biological), which can result in fatigue and a reduced ability to think and concentrate (cognitive) [26]. This may make individuals with depression less likely to participate in health-promoting behaviors such as healthy eating and exercise [41]. This loop could justify why there is a 60% increased risk of developing diabetes, specifically type 2, when also diagnosed with depression [42]. This is illustrated in a study done by Katon et al. (2009) which found that symptoms of depression were associated with fewer days of eating a healthy diet and exercising [43].

Further emphasizing the point of the behavioral connection between depression and the occurrence of diabetes was a study conducted by Golden et al. on ethnically diverse men and women, 45 to 84 years old [44]. This study looked at the relationship between depressive symptoms, associated lifestyle factors (e.g., physical inactivity, high-calorie diets), and the incidence rate of T2DM. The research findings revealed that individuals with elevated depressive symptoms had an

incidence rate of 22.0 per 1000 person-years for developing type 2 diabetes, while those without such symptoms had an incidence rate of 16.6 per 1000 person-years. Additionally, the risk of incident T2DM was 1.10 times higher for each 5-unit increment in the Center for Epidemiologic Studies Depression Scale (CES-D) score after adjustment for demographic factors and body mass index. The CES-D is a common self-reporting tool used to evaluate depression in the general population. Questions related to depression such as feelings toward mood, worthlessness, concentration, sleep, and lack of appetite are all assessed.

The biological mechanisms associated with depression are also linked to an increased risk of diabetes. An illustration of this is the association between depression and heightened activity of the hypothalamic-pituitary-adrenal (HPA) axis and sympathetic nervous system (SNS), as well as increased production of proinflammatory cytokines [41]. Elevated activity of the HPA axis and SNS leads to heightened production of the stress hormone cortisol, contributing to increased glucose production and reduced insulin sensitivity. Prolonged hypercortisolemia further raises the risk of developing metabolic syndrome, characterized by central adiposity, excessive accumulation of abdominal fat, and insulin resistance [45]. Cortisol's rise also increases one's risk of developing diabetes [7,41]. Moreover, chronic stress can trigger immune dysfunction either directly or through the activation of the HPA axis or SNS. This leads to an upsurge in the production of inflammatory cytokines that disrupt the normal functioning of pancreatic β -cells, promote insulin resistance, and consequently contribute to the onset of diabetes [31]. Studies have shown a significant association between elevated C-reactive protein (CRP), a pro-inflammatory cytokine, and diabetes risk [7,46] as well as related complications [47]. Overall, the role of behavior, biology, and cognition in the development of diabetes highlights the bidirectional relationship between diabetes and depression.

3.3. *The Effects of Diabetes on Anxiety Risk*

Growing evidence has established a synergy between diabetes and anxiety [48]. Individuals living with diabetes are at increased risk of developing anxiety because of concerns about dietary restrictions, taking several medication and insulin injections, constant checking of blood glucose, and lack of support from family and medical practitioners [49]. As such, incorporating psychological care in the management of diabetes could aid in reducing anxiety as emphasized by the International Federation of Diabetes [50,51]. In patients with diabetes, comorbid anxiety syndromes are correlated with heightened blood glucose levels, high body-mass index (BMI), and greater disability [52–54]. Cure of anxiety is linked to enhanced glycemic control [22], especially among people affected with acute anxiety [23]. Unfortunately, many people with anxiety are undiagnosed, hence untreated [55]. Undiagnosed anxiety among people with diabetes is concerning because it delays the onset of therapy for these coexisting illnesses and causes patients to get frustrated, which leads to ineffective therapeutic results [56].

The prevalence of anxiety in diabetes seems to be increasing rapidly. In one study, individuals with diabetes had a 20.6% prevalence of anxiety in 2000, and by 2004 the prevalence had risen to 42.2% [57]. In the same study, it was identified that people aged ≥ 45 were linked to a higher incidence, while females were associated with a more significant occurrence with age ≥ 45 [57]. In another study, compared to women without diabetes, women with diabetes had a greater lifetime incidence of anxiety disorders, with 50% having had an anxiety disorder at some point in their lives [33]. Moreover, both males and females showed a correlation between T2DM, obesity, and anxiety, with more than one in three women and one in five men showing signs of anxiety in research findings [58].

Most people with diabetes who are hospitalized have been observed to experience moderate to severe anxiety, sadness, or both throughout their stay [59]. Research studies have demonstrated that anxiety can influence medication adherence in patients with diabetes through its impact on self-efficacy expectations, which refers to an individual's belief in their ability to successfully carry out specific tasks or activities [60]. This can lead to worsened glucose regulation and greater difficulties in diabetes management [28]. The coexistence of diabetes and anxiety is associated with an elevated

risk of developing comorbidities, increased healthcare costs, and early morbidity and mortality [61,62].

3.4. The Effects of Anxiety on Diabetes Risk

Anxiety is a mental health disorder characterized by behavioral syndrome, fear, and feeling a sense of panic, with distinct subtypes of anxiety traits [63]. Research studies show that generalized anxiety disorder (GAD) and panic disorder are the most common mental health conditions [64]. A study examined the use of depression and anxiety screenings and each of their respective components as concurrent predictors of onset of diabetes [37]. It was noted that 24.9% of the participants with anxiety at baseline developed diabetes over 10 years [37]. Screening for both diabetes and anxiety is highly recommended for patients, as anxiety not only serves as a risk factor for the development of diabetes but can also coexist as a comorbidity [37].

In a recent study to investigate the occurrence of diabetes among individuals with anxiety, it was discovered that diabetes was more common among patients with anxiety as compared to the general population (11.89% vs. 5.92%, odds ratio, 1.23; 95% confidence interval, 1.17–1.28) [65]. The average annual occurrence of diabetes in patients with an anxiety disorder between 2006-2010 was revealed in another study demonstrating a higher prevalence of diabetes among people with anxiety disorders as contrasted with the general population (2.25% vs. 1.11%, risk ratio 1.34; 95% confidence interval, 1.28–1.41) [65].

Delving deeper into the link between anxiety and diabetes, research studies have identified gender as a contributing factor in diabetes prevalence [66]. Women are observed to be more at risk of developing diabetes than men, as women tend to have higher levels of anxiety disorders than men and men handle anxiety-related conditions differently than women [67,68]. Other discoveries have also suggested that the higher ratio of women compared to men in diabetes occurrence is due to a higher percentage of women with mental health issues [67]. In a prospective study investigating the association between mental health and diabetes, individuals with reported symptoms of anxiety and depression at baseline had a higher risk of the occurrence of T2DM at a ten-year follow-up [69]. Dealing with anxiety influences eating habits [70] and eventually results in increased adiposity and risk of developing diabetes [71]. Both anxiety and diabetes-related distress are linked to suboptimal glycemic control, decreased adherence to diabetes self-care routines, and an increased likelihood of developing diabetes complications [72]. A summary of the results of related studies on the interrelationship between diabetes and mental disorders has been reported in Table 1.

Table 1. The interrelationship between diabetes and mental disorders.

Author	Study Design	Population	Results
Rajput et al., 2016[73]	Cross-sectional, case-control study design.	Diabetes, n= 410 Healthy control, n=410	There were twice as many cases of depression and anxiety in those with T2DM compared with healthy controls (26.3% vs. 11.2%).
Tovilla-Zarete et al., 2012[74]	Cross-sectional, multi-center study	Diabetes, n= 820	48.27% were positive for depression while 55.10% showed symptoms of anxiety. Occupation and complications were associated with anxiety while glucose level and complications were correlated with depression.
Collins et al., 2009[75]	Cross-sectional study	Diabetes, n=1456	Patients with diabetes had significant levels of anxiety (32.0%) and depressive symptoms (22.4%). Poor glycaemic control and female gender were risks factors for

			higher anxiety scores. Older age and a higher socio-economic status demonstrated a protective effect, resulting in lower scores of anxiety and depression.
Shaban et al., 2006[76]	Cohort	Diabetes, $n=273$	Compared to men, women reported considerably greater mean anxiety levels. HbA1c was positively associated with anxiety and depression.
Campayo A. et al., (2010)[40]	longitudinal design	Subjects with depression, $n=379$	Severe, moderate, and untreated depression are all linked to an increased risk of developing type 2 diabetes. Although persistent depression had a greater risk than the rest.
Golden S.H. et al., (2008)[77]	Longitudinal cohort study	Analysis 1. participants without type 2 diabetes at baseline with and without depressive symptoms, $n=5201$ Analysis 2. participants without depression at baseline with and without type 2 diabetes, $n=4847$	Incidence of diabetes was correlated with baseline depressed symptoms. Impaired fasting glucose and untreated type 2 diabetes were negatively correlated with incident depressive symptoms, while treated type 2 diabetes exhibited a positive association.
Iversen et al., 2015[78]	Cohort	Depression, $n=36,031$	Depression was positively associated with diabetes.
Chien I. C & Lin C. H (2016)[65]	Prospective cohort	subjects had primary and secondary diagnoses of anxiety disorder, $n=766,427$	The prevalence of diabetes among individuals with anxiety disorders was greater than that of the general population.
Smith et al., 2018[79]	Meta analysis	anxiety, 14 studies ($n=1,760,800$)	Substantial positive correlation was shown between baseline anxiety and incidence of diabetes
Khambaty T., 2017[37]	Cohort	anxiety, $n=2,156$	Out of 2,156 patients, 558 developed diabetes over a 10-year period.
Engum A (2007)[69]	Prospective population-based study	depression and anxiety, $n=8311$	Individuals with reported baseline symptoms of depression and anxiety were more likely to develop diabetes ten years later.
Meurs et al., 2016[80]	Cohort study	Depression $n=3002$ Anxiety $n=9018$ Diabetes $n=1781$ Undiagnosed diabetes $n=786$	Diabetes was independently linked to depression in both identified and undiagnosed cases. Diabetes diagnosis was independently linked to anxiety but this association was not observed for undiagnosed cases.

3.5. Exploring the Role of Nutrition in Preventing and Managing Diabetes, Depression, and Anxiety

Poor nutritional status and unhealthy lifestyle habits have been widely acknowledged as established risk factors contributing to the pathogenesis of diabetes [81–83]. For instance, a study of

200,000 participants found that a healthy diet, characterized by a high intake of whole grains, vegetables, fruits, nuts, and a low intake of red and processed meats, was correlated with a decreased risk of T2DM [84]. Another study found that a diet high in sugar-sweetened beverages and processed foods was associated with an increased risk of diabetes [85]. Moreover, nutrition plays a crucial role in the management of diabetes and related complications [47,86–90]. A systematic review found that a Mediterranean diet, which is high in vegetables, whole grains, fruits, lean protein, and healthy fats, improved glycemic control and reduced cardiovascular risk factors in patients with T2DM [91]. Analysis of data from three European cohorts and one Canadian cohort, including 78,851 participants showed that higher protein intake was correlated with a lower risk of diabetes [92]. More specifically, plant protein intake was significantly and negatively related to the development of diabetes [93]. Other studies found that a low-carbohydrate diet was effective in improving glycemic control and reducing the need for diabetes medication in patients with T2DM [94,95].

Similarly, consuming high-quality diets is associated with improved mental health [96]. In a cross-sectional analysis involving a cohort of 3,172 adults between the ages of 18 and 55, it was observed that adhering to the Mediterranean diet exhibited a significant correlation with a decreased likelihood of experiencing psychological disorders such as depression, anxiety, and psychological distress [97]. Another study found that a high glycemic index diet is a risk factor for depression [9]. In contrast, it has been shown that a high-fiber diet improves glucose homeostasis, serum lipid profiles, inflammatory chemokines, and depression and anxiety symptoms in patients with T2DM [98]. Evaluating the effects of different sources of protein on the mental well-being of women showed that women who consumed more animal protein had a higher chance to show symptoms of depression (OR: 2.63; 95% CI: 1.45, 4.71; $P = 0.001$), stress (OR: 3.66; 95% CI: 2.06, 6.50; $p < 0.001$), and anxiety (OR: 1.83; 95% CI: 1.04, 3.22; $P = 0.03$), while no significant association was found between plant protein and these mental disorders [99]. Polyunsaturated fats have also been found to be effective in reducing symptoms of mental health disorders. For example, a randomized controlled trial found that omega-3 fatty acid supplementation significantly reduced symptoms of depression in patients with diabetes who showed mild to moderate depressive symptoms, independent of metabolic factors and disease duration [100].

Scientific evidence reveals a significant association between the consumption of ultra-processed foods and the occurrence of depression and other mental disorders [101,102]. A meta-analysis of prospective studies supports this link, indicating that higher intake of ultra-processed foods is associated with an increased risk of subsequent depression (hazard ratio: 1.22, 95%CI 1.16 to 1.28) [103]. These findings emphasize the potential detrimental impact of consuming ultra-processed foods on mental health outcomes, underscoring the importance of considering dietary choices in promoting mental well-being.

Overall, there is growing evidence to support the link between nutrition, diabetes, and mental health disorders. A healthy and balanced diet, characterized by a high intake of whole grains, fruits, vegetables, nuts, lean protein, and healthy fats, reduce the risk of diabetes, improve glycemic control in patients with diabetes, prevent and manage related complications, and improve mental health. Furthermore, certain eating behaviors, such as a high intake of fiber, a low glycemic diet, high intake of unsaturated fats including omega-3 fatty acids and plant-based proteins, may play a crucial role in reducing the risk of developing diabetes and mental health disorders and can alleviate symptoms of these diseases if existed. These findings highlight the importance of a healthy diet in promoting overall health and well-being, especially for individuals with diabetes.

4. Discussion

Existing studies show that while diabetes is a risk factor for developing depression and anxiety, depression and anxiety can also increase the risk of diabetes occurrence. It has been shown that individuals with mental disorders such as depression and anxiety are at significant risk of developing diabetes due to biological, behavioral, and cognitive factors. Furthermore, receiving a diabetes diagnosis can be a profoundly challenging experience for certain individuals, given the need for significant lifestyle modifications, continuous monitoring of blood glucose levels, adherence to

medications or daily insulin injections, regular utilization of healthcare services, and the looming possibility of developing related complications. All these unexpected life-altering experiences may cause patients to feel down, exhibit weight loss or gain, and experience sleep disturbances, fatigue, anxiety, and depressed mood, dramatically affecting their mental health and blood glucose control. Persistent worry about blood glucose management could also lead to overworking the hypothalamic pituitary adrenocortical axis, which can increase the blood glucose levels of an individual, putting individuals at a higher risk for developing diabetes or worsening management of diabetes. Although good quality health care improves diabetes conditions, diabetes comorbidities, including psychological problems and lack of a support system, could hinder the improvement of diabetes symptoms and increase the risk of developing related complications. Therefore, efforts to address psychological disorders among individuals with diabetes as well as screening individuals with mental disorders for diabetes should be emphasized for these populations.

Individuals in a depressive state may also lose their appetite to eat nutrient-dense foods or crave high-caloric foods, which could cause a further burden on diabetes management and enhance the risk of related complications. The integration of nutritional interventions should be more widely embraced to provide comprehensive support for patients with diabetes, enhance their ability to maintain optimal blood glucose control, minimize the occurrence of diabetes-related complications, augment emotional resilience in the face of diabetes, and improve quality of life.

5. Conclusion

The interplay of nutrition, diabetes, and mental disorders is complex and bidirectional. Management strategies that address the relationship between nutrition, diabetes, and mental disorders are crucial for optimizing patient outcomes. Integrated care approaches that incorporate nutrition education, lifestyle modifications, and psychological interventions have shown promising results in the prevention and management of diabetes and mental disorders.

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