RECIPROCAL ASSOCIATION BETWEEN DIABETES AND DEPRESSIVE SYMPTOMS

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Abstract

Diabetes and depression continue to be major public health burdens throughout the globe. Several studies suggest a reciprocal relationship between depression and diabetes (2): Depression occurrence is twice to thrice higher in people with diabetes mellitus when compared to non-diabetic people and they majorly remain undiagnosed (6). In contrast, depression increases the risk of diabetes and interferes with its daily self-management (2). The purpose of this review was to show the links between depression and diabetes, point out the significance of identifying depression in diabetic patients and identify the possible ways to address both diseases (6). A focused discussion of the proposed mechanisms underlying this reciprocal relationship is also provided (2). An important aspect is to understand the common origins of diabetes and depression and to get aware of this quite common comorbidity, in order to improve the outcomes of management of both diseases (6). Therefore, this review aims to highlight the most notable body of literature that dissects the various facets of the reciprocal relationship between diabetes and depression (2).

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INTRODUCTION:

Diabetes is a chronic disease that occurs either when the pancreas does not synthesize enoughinsulin or when the body cannot effectively use the insulin it produces (11) while depression is a serious mental condition that decreases mental and physical functioning and negatively affects the total quality of life (2). A modest association of baseline depressive symptoms withincident type2 diabetes was partially explained by lifestyle factors. Impaired fasting glucose and untreated type 2 diabetes mellitus were inversely associated with incident depressive symptoms, whereas treated type 2 diabetes mellitus patients showed a positive association with depressive symptoms and these associations weren't substantively affected by the adjustment for potential confounding or mediating factors (1). The prevalence of clinical depression and the presence of elevated depressive symptoms are higher among people with diabetes mellitus when compared to the general population (4)(5). These associations may be due to the increased risk of depressive symptoms in individuals with diabetes, increased risk of type 2 diabetes in individuals with depressive symptoms, or both (13).Factors inducing

Insulin resistance such as obesity-promoting health behaviors (example: physical inactivity or sedentary lifestyle, hyper caloric diets) (14,15,16,17) and activation of the neuroendocrine (18,19,20) and inflammatory reaction (21,22) (resulting in increased cortisol, catecholamine's, and cytokines) are associated to depressive symptoms leading to type 2 diabetes mellitus. A diagnosis of diabetes or the stress of dealing with its further complications might also lead to symptoms of depression (4). There are two prospective studies of adults which significantly shows that type 2 diabetes is associated with an increased risk of depressive symptoms(23,24) and there are other research which suggest that obesity

and insulin resistance, precursors to type 2 diabetes, are associated with a lower risk of developing clinical depression and depressive symptoms(25,26,27). A comorbid state with physical and mental disorder is challenging for healthcare to manage (2,3,9). Thus pressing need to understand the reciprocal association between diabetes and depression is significant in the management of both conditions and improve their medical outcomes and quality of life (1,2,3,4,5,6,7,8,9,10,11,12).

INCIDENCE

An Approximate of 15% to 20% people with diabetes are struggling with moderate to severe form of depression daily(28).In type 2 Diabetes Mellitus (T2 DM) depression is identified as a common comorbidity which rises the risk of developing cardio vascular events and death. A two way relationship is exhibited by depression and T2 DM as macro vascular complications (29).In Diabetes Mellitus particularly female patients are diagnosed with Major Depressive Disorder (MDD).In women diabetes mellitus is a major risk factor for developing depression disorder than in men with the highest width of gender gap between the age of (40-49) years. Female patients with overweight and Diabetes Mellitus are at highest risk of developing (MDD) and they should be diagnosed and monitored carefully (30).In general population, patients with diabetes are more likely to have depression. The estimated range of prevalence of depression among individuals with diabetes ranges from (9%-35%) (31). Incident depressive symptoms are inversely associated with fasting glucose impairment and untreatedT2 DM, although these patients showed a positive correlation with symptoms of depression (1).The association between T2 DM incidence and depressive symptoms was usually consistent for people at high/lower risk for diabetes and it significantly reminds even after BMI adjustment. Prevalence of

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depression may be up to three times higher in people with type1 diabetes and double in those with type 2 diabetes (3).

MECHANISM

Depression increases the prevalence or risk of future diabetes, whereas diabetes increases the prevalence or risk of future depression[6]. Among people with type 2 diabetes, those who use insulin have higher rates of depression than those who use only non-insulin drugs, diet and lifestyle measures. Risk factors for depression in general population includes female sex, their marital status, childhood trouble and social distress also included in people to diabetes (33).This does not suggest that the insulin is the cause of the condition ,but it may develop the disease and the additional treatment demands placed on a person when insulin is started.(33)

There was no difference in the incidence of depression between those with undiagnosed diabetes, those with impaired glucose metabolism, and those with normal glucose metabolism. Increased rates of depression were found only in patients diagnosed with diabetes, suggesting that knowledge of the diagnosis and burden of treating the condition and its complications may be related to symptoms of depression rather than biological mechanisms such as hyperglycemia. (33)

Type 1 diabetes and type 2 diabetes require different comorbidities because of their different treatments and age of onset. (6).Type 1 diabetes mellitus (DM1) occurs in childhood and early adulthood and requires lifelong daily insulin injections, whereas type 2 diabetes mellitus (DM2) occurs later in life, in adulthood and is associated with diet and lifestyle changes, oral medications or insulin.(6)

Depressed people are more inactive who avoid fruits and vegetables, and eat diets which are high in saturated fat and refined sugar, which may put them at an increased risk of developing type 2 diabetes. Life style factors play a major role in the risk of developing the conditions of diabetes and depression. (33)

Other common causes of DM2 and depression are lack of sleep, lack of exercise, and diet. These factors maybe a common pathway which activates and disturbs the stress system. (6)

Chronic stress stimulates the sympathetic nervous system (SNS) and the hypothalamic- pituitary-adrenal (HPA) axis, promoting the synthesis of cortisol in the adrenal cortex and adrenaline and noradrenaline in the adrenal medulla.(6).

Chronic stress has behavioral risks. Norepinephrine, cortisol, and other hormones activate the anxiety system, causing anxiety, anorexia, or bulimia. These same mediators cause reward system tachyphylaxis, leading to depression and cravings for food, other substances, or stress. (6). The HPA axis or SNS increases the production of inflammatory cytokines.

High levels of inflammatory cytokines interfere with normal pancreatic β-cell function, induce insulin resistance, and promote DM2 development. (6)

Patients with DM1 are unlike those with DM2, as they require more complicated disease management. (6) Blood sugar should be monitored frequently and insulin dosage, diet and physical activity should be adjusted accordingly. (6)

DIAGNOSIS
DIAGNOSIS OF DIABETES

- In addition to symptoms of diabetes (eg, polyuria, polydipsia, type 1 unexplained weight loss):

- Fasting blood glucose level of 7.0 mmol/L (whole blood level of 6.1 mmol/L) or random venous plasma glucose level of 11.1, whichever is lower.

- On OGTT had a plasma glucose concentration of ≥11.1 mmol/L 2 hours

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after ingesting 75 g of anhydrous glucose.

• In the absence of symptoms, diagnosis should not be based on a single glucose measurement and a confirmatory venous plasma measurement is required. On another day, at least one additional glucose test result with a value in the diabetic range is essential, either fasting, spot check, or 2-hour glucose challenge after glucose challenge. Random value on fasting is not available for diagnosis; a value of 2 hours should be used. (36)

• Using an A1C test, you may determine your typical blood sugar levels during the previous two to three months. You don't have to fast or refrain from drinking anything, which is a benefit of this method of diagnosis.

✓ Diabetes is identified when the A1C is more than or equal to 6.5%.

RESULT	A1C
Typically	less than 5.7%
Pre-diabetes	5.7% to 6.4%
Diabetes	6.5% or more

• Your fasting plasma glucose levels are measured during this test. The term "fasting" refers to refraining from eating or drinking anything other than water for at least eight hours before to the test. This examination is often conducted before breakfast first thing in the morning.

• When fasting plasma glucose levels are more than or equivalent to 126 mg/dl, diabetes is identified.

RESULT	FASTING BLOOD GLUCOSE
Usually,	less than 100 mg/dl
Pre-diabetes	100mg/dl to 125mg/dl
Diabetes	126mg/dl or more

• The Oral Glucose Tolerance Test (OGTT) is a two-hour test that measures your bloodsugar levels before and after you consume a particular sweet beverage. It reveals to the physician how your body metabolises sugar.

• When two-hour blood glucose levels are more than or equal to 200 mg/dl, diabetes isidentified.

Result	Oral Glucose Tolerance Test (OGTT)
Normal	less than 140 mg/dl
Pre-diabetes	140 to 199 mg/dl
Diabetes	200 mg/dl or higher

• When you experience severe symptoms of diabetes, you can have a blood test called Random Plasma Glucose Test at any hour of the day.

• Blood glucose levels more than or equal to 200 mg/dl are required to diagnose diabetes. (37)

DIAGNOSIS OF DEPRESSIVE DISORDER:

• Significant Depressive Episode:

A sad mood or a lack of interest or pleasure must be present, and there must be at least five depression symptoms for at least two weeks. Additionally, the symptoms must be extremely distressing or impairing.

Depressive episodes can be classified as mild, moderate, or severe, depending on the number and severity of symptoms and their impact on an individual's ability to function. (35)

• Absence of hypomanic or manic symptoms (28)

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SYMPTOMS		
	HYPOMANIA	MANIA
Duration of anepisode	4 consecutive days at least	At least 1 week
Severity	Not severe enough to mainly affect social/work/school functioning	severe impact on social/work/schoolfunctioning
Need to hospitalize	No	Possible
Occurrence	Occur in Bipolar II Can occur in Bipolar I also	Occur in Bipolar I

(32)

- An episode of minor depression:

2-4 depressive symptoms lasting for not more than two weeks-sad mood or lack of interest or enjoyment or symptoms that causes severe discomfort or impairment and nomanic or hypomanic conduct.

- Dysthymic Disorder

Depressive mood for the majority of the time for at least two years - Presence oftwo or more dysthymic symptoms - Never going more than two months without symptoms throughout a two-year period - Symptoms must cause clinically substantial distress or impairment - No severe depressive illness in the first two years - and the absence of manic, hypomanic, or mixed episodes. (28)

- CES-D

The CES-D, a 20-item questionnaire designed to evaluate depression symptoms in community groups. The CES-D items, which include sad mood, feelings of worthlessness, despair, lack of appetite, impaired attention, and sleep disruption, indicate the main elements of depression. Higher scores imply depressed symptoms that are more severe. Scores range from 0-60. We are aware that the CES-D does not measure clinical depression; rather, it measures self-reported depressive symptoms. A CES-D score of 16 or higher is having a consistently mild to moderate depression or dysthymia.

- MHI-5

Five-item Mental Health Index (MHI-5), a subscale of the SF-36, participants' mental health condition is used to evaluate anxiety, sadness, loss of behavioral/emotional control, and psychological well-being which are the four maincomponents of MHI-5. (3)

STRENGTHS:

To determine depressive status, three measures (the MHI-5 scale, antidepressant use, and physician-diagnosed depression) are used.

As it comprised of repeated measurements of both across time, as well as characterization of several diabetic complications, the study was ideally adapted to evaluate the complex relationship between depressed symptoms and type 2 diabetes.(1)

Inclusion of people with depression-related general medical disorders did not change theoutcomes and results.

LIMITATIONS:

Since the majority of the studies reviewed were cross-sectional, it is difficult to draw firm conclusions on the nature and trajectory of the relationship between diabetes and depression. The generalizability of this review's conclusions is constrained by the variety of

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measurement techniques and the lack of longitudinal data. (8)

Depressive symptoms were measured with self-report. Although the PHQ-9 is widely used, it is not a clinical assessment of major depressive disorder. (34)

Although, using a well utilized measure of depressed symptoms that has been widely used, validated, and shown to be reliable in groups that are ethnically diverse. However, some follow-ups were lost. We can learn more about the impact of depression on glucose metabolism and the risk of developing diabetes with extended follow-up.(16)(23)

The CES-D is a self-report of previous symptoms and should not be used to make a psychiatric diagnosis of depression as it was not created to evaluate clinical depression. To measure mild to severe depression and dysthymia, however, the CES-D is a useful and reliable instrument for epidemiological investigations. (1)

We had limited data on inflammatory markers and none on neuroendocrine markers, which restricted our capacity to investigate these biological possibilities in our analyses of incident type 2 diabetes and depressed symptoms. Finally, we received insufficient information on other diabetes-specific comorbidities and their severity, which made it difficult for us to assess whether this explained the observed relationship between treated type 2 diabetes and incident depressive symptoms. (1)

CONCLUSION:

The biological mechanism underlying the link between depression and Diabetes remains unclear. Diabetes and depression are two prevalent conditions that have complex etiology caused by a variety of hereditary and environmental factors. The current study adds to a growing body of evidence demonstrating a bidirectional relationship between these two major long-term disorders. However, further studies

are needed to determine the nature of the association between depression, glycemic control, and the development of diabetic complications, and to make suitable treatment recommendations. People with diabetes have a higher prevalence of depression. This study suggests that the presence of depressive symptoms is associated with a modest elevation of the risk of diabetes. Hence, to reduce the risk of these

Illnesses, appropriate lifestyle treatments such as healthy weight control and frequent physical activity are advised. Finally, these data imply that doctors should be aware of the increased risk of heightened depressed symptoms in diabetic patients and recommend routine screening for these patients for depressive symptoms.

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