

Depression and diabetes: the bidirectional relationship

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During the last decade, the psychological and psychosocial aspects of the management of chronic pathologies have been a major topic in liaison psychiatry. It is well known that comorbid depression is highly prevalent in persons diagnosed with a chronic illness.¹

Diabetes mellitus is a chronic disease that requires ongoing monitoring and treatment. It affects approximately 200 million people worldwide and its prevalence is constantly increasing.² Nearly one third of the affected population is unaware that they have the disease. Diabetes mellitus is the fifth deadliest disease in the USA, and more than a million people develop the disease each year. Economic costs associated with diabetes mellitus are estimated to be approximately \$132 billion annually.³

Epidemiologic studies conducted in both community and medical settings find that people with diabetes are more likely than others to experience depression.⁴ Depression is twice as common in patients with diabetes mellitus than in other patients in primary care settings.⁴⁻⁶ On the other hand, other studies have shown that individuals with depression were approximately twice as likely to develop type 2 diabetes than those who were not depressed, suggesting that depression is itself related to the development of diabetes.⁷

In addition, the prevalence of depression in patients with diabetes was significantly higher in women than men (28% and 18%, respectively).²

Several sociodemographic factors have been associated with the risk of depression in diabetic patients, notably young age, low socioeconomic and educational levels, being unmarried, and female gender. Additionally, several authors found that some racial and ethnic minorities are more at risk.²

Relationship between depression and diabetes

There is growing evidence regarding the bidirectional adverse interaction between diabetes and depression.

Depression leads to diabetes

A longitudinal study found that depressive symptoms at baseline were associated with an increased incidence of type 2 diabetes at follow-up over a 3-year period.²

After controlling for demographic and clinical risk factors, other studies have shown that depression is an independent risk factor for the onset of type 2 diabetes and a predictive factor for the number and severity of diabetic complications.² When one is depressive, the risk of developing diabetes increases by 37% to 60%.^{2,8}

Depression is associated with physiological abnormalities, including activation of the hypothalamic-pituitary-adrenal axis, sympathetic-adrenal system, and proinflammatory cytokines, which can induce insulin resistance and contribute to diabetes risk.⁸

Depression is also associated with poor health behaviors (ie, smoking, physical inactivity, caloric intake) that increase the

risk of type 2 diabetes.⁸ In addition, depression is also related to central obesity and potentially to impaired glucose tolerance.⁸ A relation between obesity and depression has been described in several studies. Approximately 80% of diabetic patients are obese or overweight, and therefore obesity may also play a role in the development of comorbid depression.⁹ Depression may cause obesity, for example, through changing eating patterns or reducing physical activity. But it is also possible that obesity may cause depression, for example, through the negative body image that is the result of obesity.¹⁰

Diabetes leads to depression

Some authors have evaluated diabetes as a risk factor for depression.^{4,5,11} In a large longitudinal study based on a general practice population, patients with diabetes mellitus were more likely to develop subsequent depression than people without a history of diabetes.¹

As with other severe chronic illnesses, psychological factors associated with the hardship of diabetes may trigger or enhance depressive symptoms.⁹ Most patients with diabetes experience high levels of emotional distress stemming from concerns and worries associated with their diabetes and its management.¹²

The burden of caring for diabetes, which includes managing complications, adhering to dietary restrictions, and monitoring glucose levels, can significantly diminish quality of life and contribute to affective disturbance.²

Psychological response to diabetic symptoms and complications, such as neuropathic pain and fatigue, may result in prolonged or recurrent episodes of depression as well as nonresponsiveness to treatment for depression.^{2,5}

In diabetic patients, the overall number of diabetes symptoms was linearly related to the number of major depression symptoms after controlling for objective measures of diabetes severity (ie, glycated hemoglobin and number of diabetes complications).²

Consequences of the diabetes-depression association

Depression may be an important barrier to effective diabetes management.⁵ Several studies have shown that depression has a negative impact on the outcome and prognosis of diabetic disease.^{2,4,5,7,11,14}

Patients with depression and a medical comorbidity are 3 times more likely than nondepressed, medically ill patients to be nonadherent to treatment recommendations.² A meta-analysis, based on 47 independent samples totaling over 17 000 patients, suggests that depression is significantly associated with nonadherence to diabetes treatment and decreased self-care.¹⁴ Depression has been associated with poor adherence to diet, exercise, and prescribed medication and regimens, with hyperglycemia, as well as with higher glycated hemoglobin (HbA_{1c}) levels, greater symptom burden, and greater functional impairment.

In addition, depression has been linked to the development of complications and increased mortality.^{2,5,7,11}

Depression is associated with poorer diabetes outcomes through decreases in self-care, particularly glucose self-monitoring,

and poorer adherence to oral hypoglycemic medication regimens. Lack of adherence to antihypertensive and lipid-lowering medication regimens has also been associated with depression in patients with diabetes.^{2,5,11}

Even low levels of depressive symptoms have been associated with diabetes self-care nonadherence, suggesting that improvement of the health state and outcome of diabetic patients depends on the tracking and the treatment of all major or minor depressive syndromes.²

Moreover, depression is also meaningfully linked to obesity and tobacco addiction; and these two factors were associated with increased insulin resistance and increased morbidity in patients with diabetes.^{2,10}

Comorbid depression in patients with either type 1 or type 2 diabetes is also associated with increased number and severity of diabetic symptoms and complications, such as retinopathy, nephropathy, neuropathy, vascular complications, and sexual dysfunction.²

Major depression in diabetic patients was associated with a significantly higher number of cardiovascular risk factors in the presence or absence of heart disease. In a sample of 4225 patients with diabetes, depressive diabetics were 1.5 to 2 times more likely to have 3 or more cardiovascular risk factors than patients with diabetes, but without depression.⁶

In the last decade, several authors have suggested that patients with diabetes and coexisting depression have higher all-cause mortality when compared with diabetic patients with no depression.^{4,13} In a large cohort (n=10 704), comorbid depression with diabetes was associated with an increased risk for all-cause mortality over a two-year period of approximately 36% to 38%.¹³

Total annual health care costs for Medicare patients with comorbid diabetes and depression is 4.5 times greater than for nondepressed patients with diabetes in the United States.²

Treatment

Even though depression is frequent among patients with diabetes, it remains underdiagnosed and untreated. Less than one third of cases is detected and treated with antidepressants.²

Several randomized, double-blind, placebo-controlled studies have shown the efficacy of modern antidepressants and the contribution of these medications to the improvement in prognosis and the quality of life of patients with diabetes-depression comorbidity.¹⁵⁻¹⁷

A controlled trial assessing the efficacy of cognitive behavioral therapy has also shown some results.¹⁸

Tricyclic antidepressant treatment, however, is limited because of its association with risk for arrhythmia, hypotension, and significant weight gain.²

Conclusions

There is a strong and robust bidirectional association between depression and diabetes. Each may complicate the evolution and aggravate the prognosis of the other. Most of the patients with this comorbidity are treated in primary care settings, but most of them are not diagnosed and therefore not treated.

Because of the degree of the repercussions of depression on quality of life and on the vital prognosis of patients with diabetes, as well as the risk of developing diabetes when a person is depressed, it is the duty of all physicians to track down this comorbidity and to treat it as early as possible.

CLINICAL CASE

Mrs F. A., 40, is a restaurant manager. Her type 2 diabetes mellitus was discovered 5 years ago. She reported that she had always had a weight problem. She is married and her daughter is 15 years old. Her general practitioner prescribed, on discovering her illness, a diet and oral antidiabetic medications with regular glucose self-monitoring. Three months ago, during a visit to her GP, she reported headaches and insomnia. Her blood test showed poor control of blood glucose. An eye examination and an increase in the dose of treatment were recommended.

Two weeks later, she seemed more tired. Her husband reported that she has been isolated and irritable for more than six months. He added that she had poor adherence to the diet and medication. She gained 5 kg in 2 months.

A more detailed interview revealed that she felt sad and could no longer feel pleasure. The slightest domestic upsets became unbearable. Concerning her diabetes, she felt exhausted and hopeless. She no longer wanted to continue the diet or treatment. She added that she had sexual difficulties and many disputes with her husband. She felt misunderstood. Following this consultation, an antidepressant medication was prescribed.

Two weeks later, Mrs F. A. was less irritable, slept better, and was progressively resuming her work. She was also taking her medications regularly. After a month, she began to smile again and lost about 2 kg.

After 10 weeks of antidepressant treatment, Mrs F. A. felt completely recovered from her depression. Her clinical examination and lab test showed a marked improvement and well-controlled glycemia.

MAIN POINTS

- Depression leads to diabetes mellitus and diabetes mellitus leads to depression.
- Depression can induce insulin resistance and contribute to diabetes risk via activation of the hypothalamic-pituitary-adrenal axis, sympathoadrenal system, and proinflammatory cytokines.
- Depression may be an important barrier to effective diabetes management.
- Diabetes and its complications may also contribute to poor depression outcomes.
- People with diabetes and depression are more exposed to diabetes complications and early death.
- Antidepressant therapies are effective in people with diabetes and have beneficial effects on glycemic control.

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