

## Diabetes and Depression

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### Abstract

Depression is the common psychiatric illness which is co-existing with diabetes. Depression might increase the underline inflammatory markers which are implicated in diabetes. Untreated depression can lead to worsening of diabetes and its complications. Diabetes and depression are a two way street and they need to be treated with holistic approach which include glycemic control, antidepressants and Cognitive behavioural therapy (CBT) to prevent complications. This article highlights the prevalence diabetes and depression, underlying biological mechanism and various existing approaches for effective management of both conditions.

**Keywords:** Diabetes; Depression; Psychiatric illnesses.

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### Introduction

Depression is a common psychiatric illness which co-exists among patients with diabetes. As per the World Health Organization, nearly 340 million people are affected with depression globally and 300 million people will suffer from diabetes mellitus by 2025.<sup>1,2</sup> From self-report questionnaire and diagnostic interview based studies, the correlation between diabetes and depression has been found to be between 25-35% and 9-14% respectively.<sup>3</sup> The co-occurrence of depression in diabetes can be attributed to several factors, including the psychological and psychosocial effects of the disease, a likely common genetic susceptibility and common pathophysiological abnormalities involving neuroimmunological and neuroendocrinal pathways, as well as organic microvascular brain abnormalities due to the inflammation in the brain.<sup>4</sup> Among those suffering,

the prevalence of depression was found to be higher in the lower socioeconomic class, unmarried individuals, and those with poor social support, poor glycemic control and high stressors. The prevalence was also noted to be twice as higher in women than men due to emotional lability. A special insight into the study of depression in the diabetic population of India alone showed that the correlation could be anywhere between 7-84%.<sup>5</sup>

### Biology

The correlation between diabetes and depression is a two way street. Depression is associated with significant pathophysiologic changes that may contribute to the increased susceptibility of depressed patients to Type 2 diabetes and/or complications from both Type 1 and Type 2 diabetes. Although the exact mechanisms are poorly understood despite intense research, depression

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is associated with abnormalities in metabolically significant biologic pathways. This results in increased counter-regulatory hormone release and action, alterations in glucose transport function, and increased immune inflammatory activation. Such abnormalities could contribute to insulin resistance and/or pancreatic-islet cell dysfunction thereby leading to diabetes. Once individuals are diagnosed as diabetic, exaggeration of depressive symptoms may be seen due to factors such as inability to adjust to a diabetic diet, increased lapses in filling of oral hypoglycemic medications.<sup>6</sup> It can also be attributed to functional impairment and increased expenses due to the morbidity of the diseases.<sup>6,7,8</sup> To summarize, psychological stress leads to the release of counter regulatory hormones such as glucocorticoids, growth hormone, and catecholamines which counteract the action of insulin by raising blood levels of glucose. Depression is associated with sympathoadrenal activation, hypothalamic-pituitary-adrenocortical hyperactivity, and alterations in the activity of the hypothalamic growth hormone axis. A meta-analysis of multiple cross-sectional studies.<sup>9</sup> Indicated that patients with diabetes and comorbid depression exhibit poorer glycemic control and greater prevalence of multiple diabetes complications (retinopathy, nephropathy, neuropathy, sexual dysfunction, and macrovascular complications).

### Diagnosis

In assessing the prevalence of depression, the observation of cognitive symptoms is more useful than vegetative symptoms. These include weight loss, diminished appetite, hypersomnia, psychomotor retardation, and loss of libido. It was also found that diabetics with severe depression experienced more severe symptoms of diabetes than their non-depressed counterparts. The occurrence of diabetic complications such as retinopathy, nephropathy and macrovascular complications were greater in these individuals.

### The impact of depression in diabetes

The increased burden of depression in diabetes has been associated with poor self care, reduced compliance to diabetic diet, poor glycemic control, greater chances of diabetic complications, cognitive impairment, and reduced quality of life. The self-care aspects evaluated were diet, medication, exercise, self-monitoring of blood glucose (SMBG), medical

appointments attendance and composite self-care measures. A significant association between depression and diabetic complications has been identified. Quality of life (QoL) is another concern. A systematic review on depression and QoL in patients with diabetes has concluded that QoL (both physical and mental) was significantly impaired in diabetic patients with comorbid depression.<sup>10</sup> Depression and diabetes in combination behave as a double edged sword for increasing rates of mortality due to their impacts of cardiovascular health.

### Treatment of depression in diabetes

After establishing several studies that actualize the likely correlation between diabetes and depression, one must choose a drug that not only targets glycemic control, but proves useful for the depression aspect as well.<sup>3</sup> In this regard, nortryptaline was found to decrease depression, but had a negative impact on glucose control. On the other hand, fluoxetine tended to decrease depression and improved glucose control as well by reducing hbA1C and obesity. In patients with diabetic neuropathy, Duloxetine, paroxetine, amitryptiline and desipramine have been more effective antidepressants than fluoxetine, although their advantages must be weighed over their potential side effects such as weight gain, hyperglycemia and orthostatic hypotension. The newer generation antidepressants have been a boon as they have significantly less antiadrenergic and anticholinergic effects and lack quinidine-like action and lethality in overdose. Paroxetine, but not fluoxetine may be highly effective in treating painful diabetic neuropathy.<sup>11</sup> Indeed, in a double-blind, placebo-controlled trial of non-depressed diabetic patients, paroxetine was more tolerable than imipramine but was somewhat less effective than the TCA in reducing symptoms of peripheral neuropathy.<sup>12</sup> However, it must be remembered that the SSRI's are potential inhibitors of cytochrome p450 and therefore they could alter the effectiveness of oral hypoglycemic such as, the thiazolidinedione pioglitazone, the meglitinides, repaglinide, and nateglinide. Therefore, nefazodone, fluoxetine, and fluvoxamine would be expected to confer a risk of problems with hypoglycemia. Moreover, inhibition of the CYP 2C9 isoenzyme by fluoxetine, fluvoxamine, or sertraline would also potentially interfere with CYP 2C9 metabolism of the sulfonylureas tolbutamide and glimeperide. The atypical antidepressant bupropion has minimal inhibition of CYP enzymes, is effective in the treatment of nicotine dependence, and is associated

with minimal sexual dysfunction. A holistic approach to treating depression is also including psychotherapy along with pharmacological therapy since they may help in glycemic control through neurophysiological mechanisms such as reducing stress related hormones and altering the neuropeptides related to stress, appetite and satiety. *Cognitive behavioral therapy* leads to significant improvement in HbA1c and reduces rates of depressive thoughts. Therefore including CBT along with pharmacotherapy is a well rounded approach in targeting depression in diabetics.

## Conclusion

To be a great clinician, we must not only see patients as carriers of disease who need to be treated with drugs. Ignoring the psychological burden of a disease leads to treatments that are half as effective as they would be if we saw patients as human beings and health as involving not just physical aspects, but emotional and mental aspects as well. Diabetes is a major life burden, and it is only normal to experience depression, anxiety and poor self care as a result of it. Therefore, it is important to treat the mental aspects that arise out of it. Understanding that depression by itself can increase the inflammatory markers that are implicated to cause diseases such as diabetes is a reminder of how important it is to treat depression and other psychiatric illness in their budding stages so that they don't lead to morbid diseases such as diabetes in the future. Diabetes and depression are a two way street and a double edged sword and they need to be treated with not just glycemic controls but antidepressants and CBT as well to achieve improvements in HbA1c and prevent complications such as neuropathy, retinopathy and diabetic foot. Effective treatment of depression in patients with Type 1 or Type 2 diabetes may normalize neuroendocrine and immunoinflammatory hyperactivation, facilitate psychobehavioral adherence to diet and exercise, and improve glycemic control.<sup>13</sup> Understanding this and spreading awareness of this has been the objective behind this article so that it can spread light on treating individuals as human beings and not just carriers of disease.

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