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# Examination of the Synergistic Relationship of Diabetes and Depression

Rajeev Pandey1\*, Jesse Galinski2, Jamee Charles2 and Gurumurthy3

<sup>1</sup>Department of Biochemistry, Spartan Health Sciences University, St. Lucia, West Indies <sup>2</sup>Community Health and Research Center of Spartan (CHARCOS), Spartan Health Sciences University, St. Lucia, West Indies <sup>3</sup>Department of Neurosciences, Spartan Health Sciences University, St. Lucia, West Indies

#### Abstract

Diabetes is a chronic condition affecting the physical, mental, and social aspects of a patient's life. When examining the diabetic condition, depression and its long-term sequela are just as serious as other diabetic related conditions such as congestive heart failure. In this review the authors have attempted to discuss the key factors involved in diabetic conditions associated with depression.

Keywords: Depression; Diabetes; HbA1c

#### Introduction

Diabetes has been described by the World Health Organization as "a growing epidemic" with 150 million cases estimated currently and 300 million cases estimated worldwide by 2025 [1]. Diabetes is one of the leading causes of death and disability worldwide and is divided into four major categories based on etiology: Type I, type II, gestational and other specific types. Diabetes has been shown to have serious effects on the physical, emotional, and social well being of those affected [2]. Anxiety, fear, and temporary despair are normal emotions that individuals diagnosed with diabetes may experience. However, chronic anxiety and fear, the most frequent emotional disorders reported among diabetics may further develop into major depression if other contributing variables are present [3]. Other variables contributing to depression may be in the form of numerous hospitalizations or other systemic conditions secondary to diabetes. In a recent study, depression alone was associated with increased risk for all-cause mortality with a specific 1.5 fold increase in mortality for diabetics [4]. Meta-analysis of 24 studies has established that depression is associated with hyperglycemia and a poor glycemic control [5].

It is imperative, therefore, to predict and prevent related complications in the diabetic condition to minimize the chances of developing diabetes related depression.

People with diabetes experiences significantly higher health care costs than the same populations without the condition. For example, cardiovascular disease which is a diabetic complication accounts for 70% of death rates in diabetic patients and is a major cause of Medicare costs [6]. A multivariate analysis of 1,694 adults with diabetes showed that patients with comorbid coronary heart disease (CHD), hypertension, and depression more strongly predict future costs than HbA1C levels. This 3-year cost evaluation suggests that depression is associated with a 50% increase in medical costs [6]. Heart failure and depression are both debilitating diseases that may co-exist but this does not imply causation of one via the other. Interesting to note, though, is the increased incidence of heart failure, diabetes, and depression in patients [7]. Comparison of both diabetic depressed and non diabetic depressed groups has shown that there are statistically significant differences in the quality of life between the two depressed populations. In general, the effect of depression on the quality of life in diabetics is greater than the negative effect of diabetes itself [8]. The foundation of the relationship between depression and diabetes is still unclear however several ongoing studies are geared toward exposing the link. For example, one of the studies mentioned above focuses on what is known about the stress response of the cortisol pathway and its clinical association with depression [9]. Whatever the cause, the underlying idea in recent studies is based on two questions: whether diabetes is a risk factor for depression development, or is people with depressive symptoms at risk for developing diabetes? A number of studies have shown that depression predicts the onset of serious conditions including heart disease, cancer, stroke as well as diabetes [1,10]. The knowledge that these two conditions, diabetes and depression, may co-exist, however casually, is an important aspect in the care of each and the prediction of both [11].

## Clinical Diabetic Depression and Sociological Involvement

Analysis of data from numerous studies suggests that the cormorbidity of depression and diabetes is related to different variables. Hypothesized mechanisms include genetic, biological, behavioral, and social factors [12]. Population-based studies have found that female gender, young age, lower amount of education and income predispose a person to the likely hood of depression in diabetics [1,13].

In a cross-sectional survey, diabetes persons were two times likely to have depression as individuals without diabetes. Furthermore, compared with non-depressed people with diabetes, depressed diabetic patients were less educated, more likely to be female and physically inactive. In addition, they were less likely to be employed or married and to have more comorbidity. This population had a significant number of bed days due to illness, prolonged duration of hospitalization, and multiple hospital admissions [14]. Sex interactions are important to this topic as lower quality of care for heart conditions accompanying diabetes have been documented in women while increased cardiac mortality has been shown in diabetic women [13]. Results of a population based study by Kanton et al. suggest that independent factors are associated with higher chance of meeting criteria for major depression. The criteria for developing major depression are younger age, smoking, and female, less education, unmarried, with BMI

\*Corresponding author: Dr. Rajeev Pandey, Associate Professor, Department of Biochemistry, Spartan Health Sciences University, PO Box 324, St. Lucia, West Indies, Tel: (718) 454-6126; Fax: (718) 454-6811;E-mail: rpandey@spartanmed.org

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greater than 30. In men major depression was found to be a result of similar factors including higher number of of diabetic complications. Independent factors for minor depression included younger age, less education, non-Caucasian, BMI over 30, smoking, longer duration of diabetes with higher number of complications [13].

A community study carried out in Quebec, Canada aimed at describing the progression of depression in diabetics over a three year period. Each year the patients were given a questionnaire and assessed for depression. Data from the study showed four distinct groups: No depression, slow depression, depression increased from the previous measurement, and improved depression. The results showed that roughly 33% of the diabetics involved have some sort of depression and that roughly 20% of those had depression that was increasing with time [15]. The findings above have also been isolated by other research groups [16]. Foot ulcer is an important comorbidity that influences the quality of life in people with diabetes and is associated with depression over time and increased mortality [17,18]. Also, depression might be contributed to poor disease outcome thorough physical inactivity [19]. There is growing evidence that suggests that depression can directly stimulate the production of pro-inflammatory cytokines [20], or inflammatory factors such as C-reactive proteins that influence a spectrum of conditions such as type 2 diabetes [12]. One of the hypothesized mechanisms is that high prefrontal glutamate levels may play an important role precipitating the depression presenting in diabetic patients [21].

#### Negative Effects of Depression on Patient Lifestyle

Depression affects at least 25% of diabetic patients, nearly twice the number of the general medical population. Diabetes and coexisting depression have higher all-cause mortality relative to non-depressive diabetic patients [4]. End-organ damage resulting from macrovascular and microvascular complications is a common cause of death among these populations with ischemic heart disease being the most common underlying cause of death. The risk of psychological symptoms in diabetes has been extensively researched and written about with several positive correlations between diabetes and the development of Serious Psychological Distress. This distress condition is manifest by a range of experiences that are personally troubling, confusing, or out of the ordinary [22]. Lin et al. [12] in a prospective cohort study of 4,184 patients with type II diabetes concluded that individuals with diabeticdepression face substantially elevated risks beyond cardiovascular deaths. The interaction between diabetes and depression has been found to be synergistic, predicting greater mortality, greater incidence of vascular complications, and greater incidence of functional disability in daily living activities [23].

Depression has adverse effects on energy, motivation, concentration, self-efficacy, interpersonal interactions, high hopelessness and even suicidal behavior [24,25]. One example of an adverse lifestyle effect on men is erectile dysfunction. Erectile dysfunction has been shown to have a higher incidence in diabetics than the general population. The effect of erectile dysfunction in diabetic men has been shown to generate depressive symptoms via inhibition of sexual function and to promote an overall negative self image. The management of erectile dysfunction has been revolutionized by the discovery of phosphodiesterase type-5 (PDE5) inhibitors, the first-line therapeutic options for diabetic men with erectile conditions that are efficient and safe [26]. Diabetic depression is also associated with an impaired ability to follow physician recommendations for lifestyle changes such as diet, exercise, and medication adherence [6,27]. Interesting to note is not

only the affect of diabetes on those who have the condition, but the psychological impact on parents with diabetic children. One study focused on the anxiety, quality of life, and depressive state of 70 parents who had diabetic children. This study showed that psycho-affective difficulties are frequent among parents with diabetic children due to the stress involved with the care of their child's condition [28].

## Setting Clinical Goals for Depressed Diabetic Patients

People who suffer from both diabetes and depressive disorders have less adequate glycemic control, more complications, increased medical service use, and lowered medication adherence [1]. The presence of depression seems to have a varying impact on a patient's ability to reach clinical goals such as glucose, lipid, or blood pressure control. Psychological stress associated with diabetic management may lead to elevated depressive symptoms [10].

Diabetes patients that are depressed are less likely to achieve glucose goals; however, the realization of goals improves when patients receive antidepressants in addition to their normal diabetic treatment. In two meta-analysis studies depression was found to have significant association with increased HbA1c levels and diabetic complications [13]. Findings in 1,223 adults with diabetes-depression suggest that depression symptoms make it harder to reach optimal A1c levels, but anti-depressive treatment may ameliorate this effect [29]. Studies report a clear link between mental health symptoms and poor metabolic control (high levels of HbA1c) without gender differences in youths with poorly controlled type I diabetes [30]. Also, unlike blood pressure, depression seems to make it harder to obtain the target values for lipids [29]. Close management of those diabetic patients showing depressive symptoms along with short and long-term clinical goals seems to be the key to prolonged health.

#### **Treatment Options for Diabetics with Depression**

Due to the severe impact of diabetes on the quality of life screening and treatment of depression are important for diabetic patients [8,14]. Depression is a prevalent and recurrent disorder among diabetic patients that complicates the management of the disease. Therefore, treatment of this psychiatric impairment has significant positive effects on mood and quality of life [31]. The concept of psychological treatment is reinforced by the fact that independent studies have shown that positive emotional states improve the self-management of chronic care situations [32]. Satisfactory treatment of depression has been shown to increase a patient's satisfaction with their diabetic treatment, which could lead to improvement of glycemic control [18].

The treatment of depression in diabetes is similar to the treatment of individuals who are depressed but do not have diabetes. Antidepressants, psychotherapy, or a combination of both can achieve positive results. Up to now no single treatment that leads to better medical outcome in patients with diabetic depression has been identified [33]. The selected treatment for depression dominated by somatic symptoms might be medication whereas psychotherapy would be more geared toward patients with existential difficulties [31].

Selective serotonin reuptake inhibitors are widely prescribed for patients with comorbid diabetes and depression. SSRIs have been shown to be as effective as TCAs at treating depression but have fewer side effects such as weight gain and sedation. SSRIs such as Sertraline have shown improvements in HbA1c with medication of 1 year [34]. Another group of antidepressants are the TCAs. However, TCAs can have harmful effects in diabetics such as GI distress, sexual dysfunction, and cardiovascular effects [27,31]. Other types of antidepressants such as Bupropion or Venlafaxine have also been used in these types of patients.

Psychotherapy includes several methods, such as "Cognitive behavior therapy", that have demonstrated good results in improving glycemic control [27,31,35]. Interventions with increase exercise and improve glycemic control may decreased the depressive symptoms experienced in the condition. Further, self care activities based on nutrition are important [31]. Finally, it should be noted that optimal treatment of depression in patients with diabetes may require a comprehensive approach that couples the specific depression treatment with focused efforts to improve glycemic control [31]. Effective treatment of diabetic depression, in those who suffer from it, via medication or lifestyle change, may improve the negative effects of the diabetic condition, which is likely to improve overall life outlook [36,37].

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