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# A SYSTEMATIC REVIEW OF DEPRESSION IN DIABETIC PATIENTS

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***Abstract:*** The purpose of this review is to give insight regarding the information about diabetic associated depression in the patients and associated risk factors with management approach. Individuals diagnosed with type 2 diabetes mellitus who also have comorbid depression has been linked to worse clinical profiles and is connected with depressive symptoms. An increased prevalence of depression has been associated with micro- and macrovascular issues, specifically neuropathy, nephropathy, and diabetic foot disease. Depression is more common among patients with type 2 diabetes mellitus due to a variety of variables, including pain and functional impairment, inadequate social support, poorer diabetes self-care, longer duration of diabetes, complications from diabetes, and the need for insulin therapy. Although it's not always the case, depression in diabetics has been related to ageing. Individuals over 50 were far more likely than those under 50 to show depressive symptoms in diabetic condition. There were found to be significant relationships, with a larger incidence in women, between the sex of the diabetic patients and their symptoms of stress, anxiety, and depression. Diabetes-related depression affects women more frequently than it does men. There is a positive correlation between depression and longer-term diabetes mellitus. A longer duration indicates a higher degree of depression in the patients. Pharmacologically, antidepressant drugs such selective serotonin reuptake inhibitors (SSRIs) are helpful. Dopamine reuptake inhibitors like bupropion seem to work in diabetes type 2 just like SSRIs do. Interpersonal therapy, cognitive behavioral therapy, and exercise intervention programs are examples of non-pharmacological therapies that can be used.

***Keywords-*** Depression in diabetes, Co-morbid depression, Diabetic anxiety, Risk factors, Anti-depressants.

## INTRODUCTION

Diabetes mellitus is a long-term, progressive illness that is linked to both medical and psychological comorbidities [1]. Both diabetes and depression are regarded as public health issues, impacting around 350 million individuals globally each [2][3]. Patients with diabetes, especially women, had two- or three-times greater rates of depression than the overall population or people from lower socioeconomic backgrounds. Furthermore, there is evidence linking depression in diabetics to possible clinical, lifestyle, and sociodemographic characteristics that are common to the broader community. The significance of concomitant chronic somatic disorders must be considered when examining the link depression and diabetes in relation to each other [4]. Overall, studies in the past have shown that individuals with a variety of chronic somatic illnesses have greater rates of depression. Depression tends to be more common in diabetes mellitus patients, and it raises the possibility of diabetic complications, delays wound healing, and increases mortality risk by three times within 18 months of the first foot ulcer [5]. Patients with depression frequently experience comorbid anxiety, which exacerbates how depression presents clinically. There is overlap between the markers of depression and anxiety when evaluating whether or not a person with depression also meets the criteria for an anxiety condition [6]. When coupled, the likelihood of having diabetes and depression is about twice that of random chance. Because the symptoms of depression and diabetes aggravate each other, co-occurring diseases present a significant treatment problem. Despite the availability of useful screening instruments, Diabetes patients' depression is frequently disregarded.

## REVIEW OF DIABETIC DEPRESSION

There are contradicting reports about the correlation between depression and glycemic control [7][8][9]. Depression can be brought on by inadequate glycemic management, and vice versa. The consequences of diabetes mellitus have a substantial effect on the prognosis. Micro- and macrovascular problems, in particular neuropathy, nephropathy, and diabetic foot disease, have been linked to an increased occurrence of depression.

A study conducted by Anne Engum, MD et al shows individuals with type 1 and type 2 diabetes had higher rates of depression (15.2 and 19.0%, respectively, vs. 10.7% in the nondiabetic population) when compared to the non-diabetic population. This study

concludes, when comparing the people with types 1 and type 2 DM to the non-diabetic population, the incidence of depression was significantly greater. Depression in individuals with type 2 diabetes has been connected to a number of variables, including low educational attainment, physical inactivity, subjective somatic complaints, and physical impairment. Depression was linked to both physical impairment and low levels of education in with type 1 diabetic patients. [10]

According to Bagher Larijani et al. Depression is a notable psychological complication of diabetes that is more typical in females with uncontrolled diabetes and systemic problems of the disease. Research additionally clarifies that depression was more common in persons with systemic diabetes problems than in those without such complications. 41.9% of patients had a Beck Depression Inventory diagnosis of depression. Of these patients, dysthymic disorder was confirmed in 9.3%, major depressive disorder in 23.7%, and a combination of the two diseases was found in 0.8% of cases. [11]

**Risk factors implicated in diabetic-depression**

Comorbid depression has been linked to a higher burden of medical symptoms in diabetic individuals [12].
Rahimian-Boogar I et al [13] explains that the incidence of depression in type 2 diabetic patients is influenced by a number of factors, including pain and functional disability, inadequate social support, poorer diabetes self-care, longer duration of diabetes, complications from diabetes, the need for insulin therapy, HbA1c>9%, BMI>25 kg/m2, and the experience of significant life events.

Mussa MR et al. concluded from their research that, most diabetic people experience depressive symptoms. Depression was linked to treatment compliance, diabetes retinopathy, feeling agitated or anxious, impotence, and diabetic foot ulcers. Among people observed with diabetes, the precise type of depression ranged from mild depression (30%) to severe depression (8%). Therefore, it is essential to test for depression early in diabetic patients to improve self-management and positive health outcomes. [49]

Ali SY et al. revealed in Ethiopia diabetic patients that type 2 diabetic individuals seeking follow-up therapy at the hospital had a notable depressive burden. Depression was found to be predicted by glucose management, the existence of complications, and a longer period of diabetes. As a result, all parties involved have a responsibility to enhance blood sugar regulation and encourage healthy lifestyle choices, especially for individuals who have problems or have been ill for a long time. [50]

According to Katon W et al. the increased risk of problems in older patients with mild depression may possibly be explained by the prolonged duration of diabetes in these patients, as well as their higher BMI and smoking rates. [14]. Additionally, a recent longitudinal study discovered that depression in type 2 diabetic patients was linked over time to higher risks of micro-vascular and macro-vascular problems [15]. It's also probable that for some people, depression episodes were brought on by complications from their diabetes. According to recent longitudinal epidemiological research, patients who have new functional limits as a result of their chronic illness are more prone to experience depression [16].

Yekta Z et al. conducted a study on behavioral and clinical factors linked with depression in diabetic patients, concludes that depression was most prevalent in older adults. Individuals over 50 years old had a markedly increased likelihood of experiencing symptoms of depression comparing with those under 50 years old. Although the difference between the number of women (94/205, 45.9%) and males (34/90, 37.8%) with depression scores on the BDI (Beck Depression Inventory) was not statistically noteworthy. Nevertheless, women's mean BDI scores were significantly higher than men's. This study by Yekta Z et al [17] found that, Individuals with depression had lower levels of education (81.3% against 68.3%) and lower incomes (64.1% versus 52.4%) compared to non-depressed individuals ($P < 0.05$). Additionally, there was a notable difference in married and unmarried patients; percentage of married patients with depression was higher (97.4%) than that of patients without depression (92.9%). ($P < 0.05$). The diabetic patient's depression score was unaffected by their BMI [17].

Studies by Robinson et al. and Gavard et al. diabetics who are currently depressed possess a far higher BMI than diabetics who are non-depressive [18]. Because of its correlation with inadequate glycemic control, noncompliance with diabetes therapy, and an elevated risk of micro- and macrovascular disease consequences, depression is very important when it comes to diabetes. [19].

According to Almawi W et al. study on significant correlations were found between the sex of the diabetic patients and symptoms of depression, anxiety, and stress, with a raised prevalence in women. An increased percentage of T2DM patients was observed in the groups with mild-moderate and severe-extremely severe depression, anxiety, and stress. While unemployment was linked to anxiety and depression, chronic illness and the length of the illness were strongly associated with the three disturbances by Almawi W et al. study. [28]

Ganasegeran K et al explains, in Malasia diabetic patients, anxiety was substantially correlated with age, ethnicity, and IHD (ischemic heart disease). The following factors were shown to be strongly linked to depression: age, ethnicity, and monthly household income. Based on this research, Individuals who were 50 years old or above scored higher on anxiety (9.1±4.6) than patients who were under 50 years old (6.4±2.7, $p<0.001$). Furthermore, there was a greater degree of depression (9.2±4.0) among patients who were 50 years old or older compared to younger (6.3±2.9, $p<0.001$). [20] Patients unemployed had greater depression scores (7.9±3.2) than those with employed patients (6.4±3.3, $p=0.007$). Thus, Age, ethnicity, and IHD were shown to be strongly correlated with anxiety, while age, ethnicity, and monthly household income were found to be significantly linked with depression [20].

Xu X et al. discovered that a decline in household income and visual acuity increases the potential of developing depression in diabetic retinopathy patients in China. Crucially, they also discovered a negative correlation between the patients' depression symptoms and their quality of life. Additionally, this study suggests that depression symptoms are prevalent in population with diabetic retinopathy. The results of multiple logistic regression analyses by this research pointed out important risk variables for depression, including female gender, low monthly income, impaired vision in the better eye, and history of laser therapy. [21]

Mir K et al. research tells that, age and the length of diabetes were depressive risk variables. There was no discernible relationship found between the kind of diabetes mellitus medication and depression. The results of the study indicated a correlation between depression and diabetes mellitus; that is, over half of the patients who were surveyed had moderate to severe depression. [29] Growing older and increased diabetic length are typically linked to depression. Research conducted in the West also indicates that women are more likely than men to experience depression [30][31].

Omar SM et al. mentioned that, among type 2 diabetic mellitus patients, living in a rural area, being unemployed, having co-morbid conditions, and being obese are all substantial risk factors for developing depression among Sudanese patients. Information from Omar SM et al. [22] concludes, Among T2DM patients from Sudan, depression is highly prevalent. Among T2DM patients, living in a rural area, being unemployed, having co-morbid conditions, and being obese seem to be important risk factors for developing depression. [22]

**Prevalence of depression among diabetic patients**

Depression is the second most common cause of disability globally, and individuals with diabetes are more likely to experience depression. A worldwide survey conducted through 60 countries using the ICD-10 criteria found that the one-year prevalence of depressive episodes in diabetic patients was 9.3% as compared to 3.2% in people without diabetes [23].

Firoj Al-Mamun et al. demonstrated that, among 390 Bangladeshi diabetic patients, depression was noticed in 25.9% of cases. Depression was more likely to occur in those with secondary education and those who used insulin and medication, whereas it was less common in those with business professional backgrounds and those who taking part in exercise. Study also concludes women were more probable to experience depression than men in two-fifths of diabetic patients. Better awareness and screening techniques should be used to identify and manage depression in diabetic patients since it raises the risk of unfavorable outcomes. [48]

M. Park et al. and G. E. Simon et al. gives the information that, diabetes and comorbid depression are linked with a 1.5-fold higher risk of death and a 50–75% increase in the expense of medical services. Information regarding depression co-occurring with other chronic diseases was scarce. According to this study, from 2003 to 2013, the T2DM group had a continuously higher annual prevalence of depression. All age groups showed a greater mortality hazard ratio among the depressed, while male and younger age groups showed a higher risk. [24] [25]

Hussain A et al. performed depression study in Kashmiri (in India) diabetic patients and found, the majority of diabetic people with major depressive disorder (MDD) have somewhat severe depression, not merely mild depression. Poorly regulated fasting blood sugar levels are significantly linked to MDD in diabetes, and this may have clinical implications for enhancing glycemic control, averting complications, and enhancing quality of life. [51]

Azami M. et al study in Iran describes, Iran has a significant rate of depression among its diabetic population. Therefore, regular psychology counselling is required to identify and cure these individuals' depression. An estimated 61% of Iranian diabetes patients reported having depression. The diabetic rates in the men and women were 49.7% and 65.6%, respectively [26].

The study by Bener A. et al. revealed that melancholy, anxiety, and stress symptoms are highly co-morbid with diabetes mellitus in Qatar. Anxiety symptoms were more common in people with diabetes mellitus than signs of depression and stress. Severe feelings of depression and anxiety were twice as common in diabetic cases as in healthy controls. It indicates that, diabetic associated depression is common in female patients compared to the male patients in Qatar population. The study's findings also indicate a strong correlation between diabetes and symptoms of anxiety, stress, and depression In Qatar. This study bears similarities to one conducted in Bahrain by Almawi W et al. [28]. Diabetes patients need early detection and therapeutic intervention because the condition appears to increase the chance of developing psychiatric illnesses. [27]

The results from Bener A. et al. study explains that psychiatric symptoms are associated with diabetic complications in the Qatar patients and should be monitored accordingly. Bener A. et al. study also explains, there was no discernible correlation found between the diabetes complications and the levels of stress, anxiety, or depression. Specifically, diabetic individuals had higher anxiety scores more often than depression or stress scores. [27]

Mir K et al. research shows, women were more likely than males to have depression among T2DM patients, who had an elevated occurrence of the condition. This investigation found a correlation between the depression and diabetes mellitus; in other words, almost half of the patients surveyed had moderate to severe depression. Mir K et al. analysis shows that 59.8% of diabetics have depression. Anti-diabetic medicine should be started together with appropriate depression treatment since diabetes may predispose a diabetic patient to clinically substantial depression.[29].

Li C et al. and Kendrick T et al. Data from the USA and the UK on the frequency of depression in diabetic patients show that the prevalence is between 30 to 83%. Similarly, A study conducted in Iran found that 55% of diabetics had depression [34]. Based on a meta-analysis conducted by Anderson et al., 8–61% of diabetics have depression [35]. As per Li C et al. People with diabetes had a high development of major depression; the prevalence rate varied significantly depending on the type of diabetes and demographic factors. [32] [33]

**Management of diabetic depression**

DA (dopamine) has a substantial effect on T2DM and depression. There is proof that T2DM and obese rodent models have decreased dopamine signaling in the striatum, which may lead to reduced psychomotor activity, motivation, and reward system dysfunction [39].

In addition to its anti-depressive qualities, Dopamine improves insulin sensitivity and glucose regulation [40]. According to studies, treating comorbid depression and type 2 DM jointly is more successful when done as part of an integrated approach [36].

Markowitz S et al found in 2011 that, A Dopamine reuptake inhibitor called bupropion would seem to work in type 2 diabetes just as well as SSRIs. Lustman PJ et al [37] has been demonstrated that pharmacological treatment with antidepressant drugs, such as SSRIs (selective serotonin reuptake inhibitors), is effective. [38] Exercise intervention programmers, interpersonal therapy, and CBT (cognitive behavioral therapy) are examples of non-pharmacological therapies that can be given [41][42][43].

Lustman PJ et al. tells, Cognitive behavioral counselling, problem-solving methods, and behavioral tactics are all used in CBT treatment. This study also demonstrated that CBT is beneficial in addition to diabetes education; 58.3% of patients in the cognitive behavioral counselling group achieved remission, compared to 25.9% of patients who just received diabetes education. This Lustman PJ et al. research also tells that, cognitive behavior therapy and selective serotonin reuptake inhibitors are weight neutral and have been linked to glycemic improvement in certain trials. Psychotherapy and medication are helpful when diabetes is present.[44]

Mota-Pereira J et al explains, physical activity alleviates symptoms of depression. The activation of dopamine and striatal pathways for the reward and the stress resistance may be partly responsible for this. Madden KM et al. [46] and Snowling NJ et al. [47] detected Exercise also enhances glycemic management, insulin sensitivity, and glucose disposal. Treatment-resistant major depressive disorder patients' depression and functioning metrics improved after a 12-week home-based exercise program consisting of five days a week of 30- to 45-minute walks. This program also helped 26% of these patients achieve remission. [45]

## CONCLUSION

In conclusion, depression is the second most common cause of disability globally, and individuals with diabetes are more likely to experience depression. Comorbid depression in patients with type 2 diabetes mellitus has been afiliated with worse clinical profiles and is connected with depressive symptoms. Many factors, such as pain and functional impairment, insufficient social support, worse diabetes self-care, longer duration of diabetes, complications from diabetes, and the requirement for insulin therapy, all have an influence on the occurrence of depression in type 2 diabetes mellitus people. When compared to people under 50, those over 50 had a much higher chance of exhibiting signals of depression in diabetic conditions. Significant relationships were discovered, with a higher frequency in women, between the sex of the diabetic patients and their feelings of stress, anxiety, and depression. Compared to men, women exhibit higher rates of diabetes-related depression. Growing older is not always, but it is occasionally linked to depression in people with diabetes. Depression has a favorable link with longer duration of diabetes mellitus. Increased long duration shows high level of depression in patients.

Antidepressant medications, such as selective serotonin reuptake inhibitors, are useful when used pharmacologically. Bupropion, a dopamine reuptake inhibitor, appears to function in type 2 diabetes exactly as well as SSRIs. Non-pharmacological therapies that can be performed include exercise intervention programs, interpersonal therapy, and cognitive behavioral therapy. Cognitive behavioral counselling, problem-solving methods, and behavioral tactics are all used in Cognitive Behavioral Therapy.

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