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The relationship between diabetes and depression (review)

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Abstract. Diabetes Mellitus seems to be the most common disease that affects almost everyone in the world. From kids to adults to senior citizens. Diabetes is a chronic condition that occurs when the pancreas does not produce enough insulin or when the body does not use the produced insulin effectively. Insulin is a hormone that controls the blood sugar level. Majority of the food we eat is converted into glucose which will then be released into the bloodstream for the use of the body. However, when there is far too much glucose in the bloodstream, it sends a signal to the pancreas to produce small clusters of cells called islets of Langerhans which consists of β-cells which secrets insulin directly into the bloodstream. When there is far too much sugar in the body when there is insufficient insulin or when the cells stop responding to the insulin, this can lead to health issues such as heart disease, vision loss and kidney disease. Depression on the other hand known as major depressive disorder or clinical depression is very common mood disorder that has a negative impact on how we feel, think and act. Striking at any age, it causes a variety of physical and emotional problems to the extent where one may not feel life isn't worth living. Though the relationship between diabetes and depression may very well lead to several other diseases, the relationship between the two can be controlled by either limiting the factors of one another or simultaneously treating both. There are many evidences that no doubt shows the correlation between diabetes and depression. This article introduces and discusses the relationship between diabetes mellitus and depression.

Keywords: diabetes, depression, stress, insulin, patient, psychology

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Особенности взаимосвязи между диабетом и депрессией (обзор литературы)

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Аннотация. Одним из самых распространенных заболеваний в современном мире является сахарный диабет, с которым живут все возрастные категории населения. Хроническое течение заболевания обусловлено тем, что поджелудочная железа не способна вырабатывать достаточное количество инсулина или, наоборот, когда организм не способен переработать его самостоятельно. Гормон «инсулин» контролирует уровень сахара в крови. Большинство продуктов, поглощаемых организмом ежедневно, преобразуется в глюкозу, которая становится источником энергии для всего организма. Когда уровень глюкозы в крови становится выше нормального, поджелудочная железа начинает вырабатывать эндокринные клетки, расположенные в островках Лангерганса, состоящих из β-клеток,

которые секретируют инсулин. Когда в крови наблюдается значительное превышение уровня глюкозы, возникает недостаточность инсулина или клетки прекращают реагировать на инсулин, что приводит к развитию заболеваний, таких как потеря зрения, почечная недостаточность или болезни сердца. Американское психиатрическое общество считает, что депрессия, будучи самым распространённым психическим заболеванием человечества, изменяет не просто самоощущение, но образ мыслей и поведение. У пациентов с диабетом наблюдается развитие депрессии, которая проявляется в изменении экзистенциального состояния человека. Авторы статьи анализируют зарубежные исследования, касающиеся взаимосвязи диабета и депрессии, которые могут привести к развитию комплексных заболеваний, а также способы контроля детерминирующих к ним факторов.

Ключевые слова: диабет, депрессия, стресс, инсулин, пациент, психология

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Introduction

Diabetes affects approximately 422 million people worldwide whether they are from low- or middle-income countries. It is also responsible for the death of 1.6 million per year and the number of cases increases steadily where this number is said to be rises in estimation to 700 million by 2045 [International Diabetes Federation, 2021]. There are several types of diabetes. Among them are type 1 diabetes, type 2 diabetes as well as gestational diabetes.

Type 1 diabetes affects the body when it does not produce insulin effectively when the blood glucose level is high [American Diabetes Association, 2021; WHO, 2021b; 17]. Different factors, such as genetics, some viruses and even environmental factors, may contribute to it. Although insulin-dependent diabetes usually appears during childhood or adolescence, it can develop in adults. Despite active research, this diabetes has no cure. So-called juvenile diabetes complications can affect major organs in the body, including nerves, eyes and kidneys etc.

Type 2 diabetes is well-known for its occurrence when the body fails to use insulin properly. Usually before developing type 2 diabetes mellitus a person will develop prediabetes which is always asymptomatic [Centers for Disease Control and Prevention, 2016]. In most countries, the fraction of people who developed type 2 diabetes are increasing where one in every 5 people over the age of 65 have diabetes. Gestational diabetes is a type of diabetes that develops during pregnancy. Women who have gestational diabetes are more likely to have complications all throughout their pregnancy and birth. However, this type of diabetes usually passes after infant has been delivered [Centers for Disease Control and Prevention, 2016]. Diabetes diagnosed throughout pregnancy can sometimes lead to type 2 diabetes. On average, more than 20 million births which is 1 in every six live births are affected by diabetes and are at risk of developing type 2 diabetes [National Institute of Diabetes and Digestive and Kidney Diseases, 2016; American Diabetes Association, 2021; WHO, 2021b].

As dangerous as diabetes is, they are not asymptomatic. Among the symptoms of diabetes are depending on how high blood sugar level is, meaning the intensity of the symptoms to be able to show. Some people may not experience symptoms at all as in prediabetes, however some symptoms tend to appear quickly and are extreme. Among them are increased thirst, increased urination, gnawing hunger, vision problems, unexplained or sudden weight loss, slow healing ulcerations or recurrent infections. Gum or skin infections as well as vaginal infections can be among the symptoms of diabetes as well [Mayo Clinic, 2020b].

The American Psychiatric Association Diagnostic and Statistical Manual of Mental Disorders (DSM-5) defines diabetes as a mood disorder that reunites various symptoms that amend the functionality of an individual. Depression disturbs cognition, emotions, and behaviours. According to DSM–5, the diagnostic criteria for a major depressive disorder consist of a core symptom such

as mood (irritable or diminished) or decreased pleasure or interest. Also it should have four symptoms as minimum amongst the following: suicidal thoughts or thoughts about death, concentration problems, feelings of guilt or worthlessness, weight loss or weight gain, fatigue or loss of energy, psychomotor retardation or change in activity, hypersomnia or insomnia lasting for at least two weeks. Depression could be described based on its episodes such as a first episode, a recurrent or chronic episode. As well, it could vary from severe to mild, having or not psychotic features.

Depression oppositely has effect where we may have difficulty performing routine daily activities. Depression may necessitate long term therapy and can strike at any age [Mayo Clinic, 2020]. It's about 50 % of risk to have a mental disorder that may lead to a drop in employment, productivity and wages even [OECD, 2014]. Depression is now widely recognised in children and teenagers but mostly in adulthood where it is estimated that 5 % of adults suffer from it. There are 264 million people in a year suffering from anxiety disorder as the result of depression and 788,000 people died of suicide as of 2015. Research reveals that about one in seven youths with type 1 diabetes meets the clinical cutoff for depression; this rate is nearly double that for youths without diabetes [McGill, Volkening, Pober and al., 2018]. Statistically, among men and women in adults 5 % of women suffer depression whereas 3 % of men suffer from depression which shows that it is a common disorder among women than in men [U.S. Department of Health and Human Services, 2018]. Depression and anxiety takes the 4th place amongst risk factors, while diabetes does only the 8th speaking of disability adjusted life years in developed countries. Depression in middle aged and elderly people however, can co-occur with other serious medical illnesses such as cancer, diabetes or even Parkinson's disease. When depression is present these illnesses are exacerbated. Diabetes-specific concerns involve fear of hypoglycemia or hyperglycemia, anxiety, and disordered eating. Chronic psychological stress has been associated with higher A1C (or glycohemoglobin), and can lead to difficulties in diabetes treatment [Stetson, Minges, Richardson, 2017]. Among the symptoms of a depressive person is they may suffer from anxious or persistent sad mood, feeling of hopelessness, loss on interest, feelings of guilt, difficulty concentrating, decreased energy or fatigue, suicide attempts, oversleeping, appetite loss and constant aches, pains and headaches. It becomes hard to «держать себя в руках, ощущать взгляды прохожих, проявлять самость, «другость»» ("keep it together, feel the passers-by on oneself and express self, *otherness*") [Filippovich, 2020, p. 62]. However, not everyone who are depressed express these symptoms and some may few are some may have all [WHO, 2021a]. The magnitude, frequency and duration of symptoms all vary from individual to individual and his or her specific illness.

Relationship between Diabetes and Depression

Diabetes produces structural changes in the brain: lacunar infarcts and cerebral atrophy, blood flow changes of both hyper- and hyporperfusion [BenAri, Ori & Efrati and al., 2020]. Among patients with diabetes it was found that brain volumes were reduced to the hippocampus. Simultaneously, an inverse relationship between hippocampal volume and glycemic control was present. Depression is associated with all the neurodegenerative processes, especially at the level of hippocampus and the prefrontal cortex. Depression has a synergistic effect in patients with type 1 and 2 diabetes, increasing the risk for complications of predicting greater mortality and increased hyperglycemia.

Diabetes and depression though are two very different illness they are actually related in many different ways. There are several evidences that show the relationship between diabetes and depression. It is to be said that diabetes patients are twice as likely as non – diabetic individuals to experience depression and vice versa. This comes down to the questions does diabetes predict depression or does depression predict diabetes [Alzoubi, 2018]. Similar to the question of does the egg or the chicken come first, it is proven that indeed there is a strong correlation between both diabetes and depression. However, there is also a question of does diabetes type 1 and type 2 affect the patient in terms of depression differently. Based on a talk by Sherita Golden

from John Hopkins Medicine, 15 to 20 % of adolescents with type 1 diabetes have elevated depressive symptoms and 23 % have subclinical depressive symptoms. A US based epidemiological study on diabetes in children and adolescents show similar rates of depression in type 1 and type 2 diabetes however it is highest in type 2. It is shown that type 1 diabetes is rather prone to occure in children and adolescents whereas type 2 diabetes is more common in middle age.

The first wave of depression occurs at the end of adolescents whereas the second wave of depression occurs at mid-life. Having a background of increased number of diabetes-specific family conflict, there was rather more reported diabetes-specific burden which was associated with problematic emotional functioning for the youth. Parents or caregivers who are more stressed by diabetes management may provide less support, therefore promoting difficult emotional functioning [Akbarizadeh, Naderi Far, Ghaljaei, 2022].

In a question of does diabetes predict depression, through observation and experience of a type 2 diabetes patient, the patient spends so much time trying to figure out what food to eat, taking medications properly, checking the blood sugar level which has become a daily routine where the patient got frustrated ad had to see a psychologist [Diabetes UK, 2019]. A low socioeconomic status is number one factor that increases the odds for type 2 diabetes [Agardh, Allebeck, Hallqvist, Moradi, Sidorchuk, 2011], meanwhile it also appears to be a cause for depression [Elwell-Sutton, Folb, Clark, Fairall, Lund, & Bachmann, 2019]. Amongst other common causes for depression and type 2 diabetes, it were found such as poor diet, lack of physical activity or poor sleep. Taking into consideration these factors, a key candidate for a common pathway could be the activation and disturbance of the stress system. This gives and overview on the prediction of depression by diabetes. Hypothesizing, depression risk can be increased by the psychological burden imposed by the disease on the patient particularly if it is associated with a set of complication especially if it is functional impairment, setting of lack of social support and a passive coping skill. Hyperglycaemia also plays a vital role in the cause of diabetes as well as may be the cause of depression. This is because it affects the part of the brain that controls mood and cognition. Chronic stress has behavioral outcomes: cortisol, noradrenalin and other hormones activate the fear system determining anorexia, or anxiety hyperphagia. These hormones cause tachyphylaxis of the reward system. It means that mediators triggers to produce cravings for food or stress and, then, depression. Excess cortisol disturbs neurogenesis in the hippocampus [Hill, Spencer-Segal, 2021], a region involved in depression as well as in type 2 diabetes [Moulton, Costafreda, Horton, Ismail, Fu, 2015]. Research has been done proved that individuals with diabetes at baseline had a higher risk of developing depression during follow up compared to those without depression of course, considering the differences and indifferences which can be obesity and socioeconomic status.

In a question of does depression predict diabetes, there are several plausible mechanisms that is depression the psychological burden of diseases leads through obesity and through a variety of other mechanism, there are also behavioural aspects where individuals who are depressed don't like to exercise tend to overeat and etc. In addition, certain treatments for depression may be the sole cause of diabetes and may induce obesity in a way of resisting insulin which is the main cause of diabetes. Stress can affect hormonal level and factors that can increase the risk of diabetes. It works by affecting the hypothalamic pituitary adrenal axis (HPA axis) hyperactivity causing an increase in cortisol level. Cortisol is the primary stress hormone which increases blood sugar level and enhances the use of glucose as well as increasing the availability of substances that repair tissues [Mayo Clinic, 2021]. In another way, stress can cause the activation of the sympathetic nervous system (SNS) which is a fundamental physiological response to stressful situations like the flight or fight response in conditions of hypovolemia, hypoglycaemia, hypoxia or cardiovascular dysfunction. This further leads to an increase in the interleukin-6-multifunctional-cytokine in the body which plays a central role in host defence situations due to its wide range of immune and hematopoietic activities [Chowdhury, 2018]. This response immediately causes resistance to insulin which then lead to the body not being able to produce and use insulin for reducing the blood sugar level leading to diabetes mellitus [Golden, 2016].

Causes of Diabetes and Depression that may be the Basis of its Correlation

As discussed earlier thought depression and diabetes are correlated and may as easily may be the cause of one another, there are also several other reasons that can cause both diabetes and depression. Amongst them are lifestyle factors and adherence. It is hypothesised that lifestyle factors are essentials speaking of reinforce the comorbidity of depression and diabetes. For instance, depressive people are more likely to be sedentary and to consume diets high in fats especially saturated fats and refined sugars totally avoiding healthy food and vitamin sources like vegetables and fruits which in turn can lead to an increased risk of diabetes. Non-compliance with self-management has also been discovered in people who have already been diagnosed with diabetes and experience depressive symptoms. There was provided a meta-analysis of over 47 independent samples that helped to find depression was essentially associated with nonadherence to diabetes treatment program that include overlooked diet, exercise or medication use, glucose monitoring. As many depressive symptoms increases as a higher risk of nonadherence to intake of fruit and vegetables. This raises the possibility of a mutually reinforcing phenomenon in which poorer self-care adherence may increase blood glucose. As the consequence, it may contribute to depressive symptoms and decreased adherence to self-care behaviours [Qiu, Cai, Zheng, Qiu, Ke and Huang, 2021].

Not only the psychological impact of the disease plays a role in causing both diabetes and depression, it is found that having diabetes can actually change the brain structure and function. In addition to the psychosocial models, diabetes and depression is very well known by now that they share a different variety of biological mechanism that can increase the risk of other conditions. Tt is known that both hypoglycaemia and hyperglycaemia have significant effects on functions of the brain like cognition and mood. Prefrontal glutamate glutamine gamma aminobutyric acid levels in people with diabetes are high than in a healthy individual based on Magnetic resonance imaging (MRI) scans correlating with depressive symptoms. Furthermore, animal studies have also shown that diabetes has a negative impact on hippocampus – dependent integrity and neurogenesis. It may interact with other aspects of neuroplasticity and contribute to diabetes-related symptom severity. In humans, hippocampal neurogenesis can be assessed indirectly using MRI, and diabetes causes hippocampal atrophy [Qiu, Cai, Zheng, Qiu, Ke and Huang, 2021].

In addition to lifestyle factors and adherence as well as brain structure and function, the impact of the external environment may also contribute to diabetes and depression. The environmental factors tend to change from the intrauterine environment to the surrounding community can very much influence the risk of comorbidity. There is compelling evidence that an individual's intrauterine environment can predispose them to type 2 diabetes. The research examining the relationship between an adverse intrauterine environment and the risk of adult depression are less definitive, but some studies have suggested a positive association while others show no association. In human studies, programming of the HPA axis and elevated cortisol excitability in childhood, teenage years, and adulthood that may result in predispose the individual to metabolic and stress-related disorders. It also has been observed following respectively low birth weight and foetal cortisol excessive exposure due to maternal stress. Several external conditions, such as childhood adversity, local neighbourhood environment, and poverty, influence the risk of depression and diabetes. Inadequate physical environments (i.e. noise or decreased walkability) and social environments (i.e. lower social capital or decreased residential stability) are linked to poor diet and physical activity patterns. Therefore, we can state a probable obesity, diabetes, hypertension, and depression as an outcome. [Subba, Sandhir, Singh, Mallick, Mondal, 2021].

Consequences of Depression in Diabetes patient

The relationship of diabetes and depression cannot be fully understood; however, it is obvious that the managements of diabetes can lead to depression. Generally, it is known that diabetes can lead to complications in health issues like oedema, nerve damage, kidney damage, Alzheimer disease as well as many others, it may as well exacerbate the symptoms of depression.

On the other hand, depression can lead to unhealthy lifestyle like unhealthy eating habits, less exercise, smoking as well as gain of excess weight which are all risk factors of diabetes. In addition to that, depression can very well impair our ability to complete daily task efficiently and effectively, communicate properly as well as think clearly. This can jeopardise our ability to properly manage diabetes leading to many other health issues as well as impact a person ability to take responsibility for their own self-care negatively [Mayo Clinic, 2020a]. This in turn may lead to poor glycaemic control and an increased risk of diabetic complication with reduced function and increased mortality. Complications of reduced functions include a significantly increased risk of dementia in older people with comorbid depression and diabetes compared to those with diabetes but no depression. For instance, a Canadian study of 1,064 people with diabetes found that the risk if poor function and reduced quality of life was approximately three times higher for those who had depressive episodes compared to those who had no or minimal depression when followed up after five years. Complication of increased mortality on the other hand include patients who have comorbid diabetes and depression. Thus, the risk of cardiovascular disease and all-cause mortality rates are 1.4 and 1.5 times higher respectively than in people with diabetes alone [Chowdhury, Sumon & Barua, Shangkar, 2018]. Depression, even mild depression, is linked to an increased risk of death due to a variety of physical conditions [Subba, Sandhir, Singh, Mallick, Mondal, 2021]. Depressive symptoms have been proven to be linked with higher blood glucose level and diabetes complication such as coronary heart disease.

Depression in diabetic patient is associated with significant additional functional fiscal and psychological cost according to growing evidences [de Groot, Kushnick, 2010]. Research examining the relationship between depressive episodes and glycaemic control in adults have generated contradictory results, with some indicating that depression has been associated with a small degradation in glycated haemoglobin while others show no effect. There is a clearer link between depressive symptoms and poorer blood glucose control in children and young adults [Subba, Sandhir, Singh, Mallick, Mondal, 2021].

Summary

Though the relationship between diabetes and depression may very well lead to several other diseases, the relationship between the two can be controlled by either limiting the factors of one another or simultaneously treating both. There are several treatments and ways of coping of depression in diabetes patients. Among them are psychotherapy and antidepressants medications. Despite the high cost, this traditional treatment has been proven in several cases to be able to help effectively in the short-term treatment of depression. Examples of antidepressant medications are Selective serotonin reuptake inhibitor (SSRI) and serotonin norepinephrine reuptake inhibitor (SNRI) [Jovinally, 2018].

In addition to that, problem solving therapies are also another efficient way to help treat the disease as it has and integrated treating system withing the primary care and has reported several advancements in depression resulting in better diabetes care. Diabetes self-management programs are also another way of treating depression ins diabetes patient as it is a programme that focuses on behavioural aspects and are successful in assisting people to improve their metabolic control and fitness level. This simultaneously manages weight loss and the risk factors of other cardiovascular disease. Regular exercise can help alleviate symptoms of diabetes and depression by increasing the so-called “feel-good” chemicals in the brain which is serotonin and endorphins stimulating the formation of new brain cells the same way and anti-depressant medication works. Diabetes and depression may be linked in many ways and we might never know that we are the sole cause if either one of the diseases.

Therefore, it is important for us to take care of ourselves as simple as changing our lifestyle to a healthier one to prevent even more chronic disease from the small ones we develop now. The typical way of curbing all disease is the most important, simple and cost-free way of treatment

which is a simple lifestyle change [de Groot, Kushnick, 2010; Jovinally, 2018; Khalooei, 2019; Mayo Clinic, 2020a]. This includes eating a balanced diet, attempting to keep a regular sleep schedule as well as working to reduce or better manage stressors and seeking support from family members and friends. To encapsulate, our review demonstrates that there is a strong correlation between diabetes and depression because it is proven that depression is very well the cause of diabetes and vice versa as there are many evidences that manifest the cause of each of these problems.

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