REVIEW ARTICLE

THE INFLUENCE OF DIABETES ON THE EMERGENCE OF EMOTIONAL DISORDERS: A LITERATURE REVIEW

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Abstract

Introduction: People with diabetes mellitus are more likely to have emotional or behavioral problems than others without diabetes. Glycemic regulation aims at the prevention of complications. However, the manner in which people with diabetes take care of their disease varies substantially, and not all nonadherence reflects an underlying psychosocial problem.

Aim: The aim of this literature review was to research the recent bibliography about the association between depressive disorders and diabetes.

Methods: An extensive review in Greek and international literature was done in valid databases (PubMed, Cochrane Library, CINAHL, Science Direct) from 2000. The search was performed with the use of key-words (MeSH terms) like: depressive symptoms, diabetes mellitus, diabetes complications, comorbidity.

Results: Diabetes is a major cause of mortality, physical disability, financial expenditure and low financial development. Complications are caused because smaller and bigger blood vessels are affected. Macroangiopathy leads to coronary disease, stroke and peripheral angiopathy. Microangiopathy may lead to retinopathy, kidney disease and polyneuropathy. Those complications may lead to higher morbidity and could lead to eye sight loss, end stage renal failure and lower extremity amputation. Depression is the most common mental disorder in the general population. One out of ten people will be affected by depression at some point. Today depressive disorder takes the fourth position and it has been estimated that it will take the second position by 2020. Depressive disorder can emerge at any point between childhood and old age but half the cases are people aged 20-50 years. Depression is 2 to 3 times more common in diabetic patients, reaching 10-20% of type 1 and 2 diabetics.

Conclusions: The strenuous daily efforts for diabetes management can create the opportunity for depression to emerge. Tertiary prevention programs can also limit the emergence of complications via early detection and treatment. Continuing education, through group or individual programs, can help with the management of diabetes and can also help with the psychosocial support of patients and families, by improving their quality of life and their mental and emotional state.

Keywords: Depressive symptoms, diabetes mellitus, diabetes complications, comorbidity

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Introduction

Diabetes mellitus is a chronic condition that may remain silent for a long time. The patients' subjective complaints are often linked to objective findings, and the development of the disease is unpredictable since there is no final cure. Nevertheless, it can be regulated with proper treatment and with the patients' "discipline" regarding their lifestyles. Glycemic regulation aims at the prevention of complications. Many diabetic patients at first (and later on) are given a plethora of information and advice, several medicines and a series of medical examinations that can usually create a feeling of helplessness and unstable emotional state. Depression occurs more often in diabetic persons than the general population. But most of the time this problem is not acknowledged since diabetes is related to stressful events that can trigger anxiety, frustration and sadness and can lead to emotional burn out.

Diabetes is a major public health issue for all healthcare systems worldwide. Each new edition of the Diabetes Atlas confirms that diabetes cases are increasing all over the world. Type 2 diabetes is not a characteristic of developed countries, since it is increasing in developing countries as well. According to WHO data, in 1995 there were 135 million diabetic patients worldwide, in 2000 there were 171 million patients and in 2006 there were 230 million diabetic persons[1,2]. The International Diabetes Federation (IDF) suggests that in 2011, 4.6 million people aged 20-79 years died because of diabetes, making up 8.2% of global mortality and being almost equal to mortality rates due to infectious diseases[3]. International epidemiological data have shown that in 2012 the diabetic population was over 371 million people, and half of them had been undiagnosed. Diabetes-related deaths have been estimated to be around 4.8 million cases, and more than 471 billion USD were spent in 2012 on healthcare for diabetes and related complications[3]. The WHO has estimated that by 2025, the diabetic population will have risen by 54.5% [1,4]. 80% of diabetic people live in developing countries and 46% of them are 40-59 years old[5,6].

According to the Diabetes Atlas, in Greece, 7.43% of adults were diabetic in 2012 (compared to 8.6% in 2007), in other words about 638.770 people, while by 2025 diabetic persons will be almost 9.7% of the total population[3,7]. The IDF has estimated that 265.540 Greek diabetic patients remain undiagnosed, with most of them being 60-79 years old, while the majority live in one of the major cities[3]. Observational studies of the past two decades have shown that self-reported diabetes rates have risen from 2.4% to 3.1% between 1974 and 1990[8], while according to the ATTICA study (2001-2006), type 2 diabetes prevalence was 7.6% in males and 5.9% in females[9,10].

The financial aspect

Diabetes is a major cause of mortality, physical disability, financial expenditure and low financial development. Healthcare spending on diabetes treatment and related complications in 2007 was as high as 232 billion USD, and in 2010 it was 376 billion USD; according to the IDF projections for 2030 it will have soared to 490 billion USD, 30-35% up, if the diabetic population will have increased as estimated[3]. The IDF has also suggested that by 2025 13% of healthcare

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spending worldwide will be on diabetes. In wealthier countries more than 80% of healthcare spending is on diabetes, in contrast with what happens in low-income countries. Almost 25% of diabetes-related spending in developed countries goes to blood sugar monitoring and another 25% goes to long-term complications. The remaining 50% is about other diabetes-related expenditures such as the prevention of micro- and macro-vascular complications. Also, patients suffering from serious diabetic complications often spend three times more money on treatment than those who stay without any complications[11].

Indirect healthcare costs, such as inability to work, early retirement and morbidity almost reach direct diabetes treatment costs. Almost a quarter of diabetes-related expenditures comes from Europe. For example, the WHO has projected that between 2005-2015[1] loss in national income because if diabetes and related cardiovascular diseases, will reach 557 billion USD in China, 303 billion USD in Russia, USD 336 billion in India, 49 billion USD in Brazil and 2 billion USD in Tanzania. The above-mentioned losses are the result of early deaths and working inability[12]. In Greece, average cost per patient was estimated to be 1300 Euros annually on the basis of current diabetes treatment costs. Patients with well-regulated diabetes have an average cost of 983 Euros annually, yet patients with poorly-regulated diabetes have a cost of 1570 Euros per annum. Overall it has been estimated that in Greece total expenditures for diabetes treatment, excluding complications, are almost 1 billion Euros annually[13].

Although diabetes is not an 'expensive' disease for individual patients, its high prevalence leads to overall high expenditures that over the years, and since diabetes becomes more and more frequent and because of shifts in the population pyramid, those expenditures put bigger pressure on healthcare finances worldwide.

Chronic Complications of Diabetes

Diabetes is a chronic condition that may lead to complications in about 30% of all cases. Complications are caused because smaller and bigger blood vessels are affected. Macroangiopathy leads to coronary disease, stroke and peripheral angiopathy. Microangiopathy may lead to retinopathy, kidney disease, polyneuropathy (gastroparesis, diarrhea, constipation, painless myocardial ischemia, postural hypotension, diabetic foot, etc). Those complications may lead to higher morbidity and could lead to eye sight loss, end stage renal failure and lower extremity amputation[14-16].

It has been suggested that those complications could be sharing a common mechanism, which is related to intracellular changes due to the patients' impaired glucose metabolism. In spite of common risk factors (hypertension, hyperglycemia and dyslipidemia) that point towards a poor prognosis and have to be dealt with immediately, there seems to be that those complications are related to each other too: the emergence of one complication seems to promote the emergence of another. Initially, some of those complications remain asymptomatic and do not occur in all diabetic patients. Nevertheless, they become more common the older the patients get and the longer their diabetes exists. But they can be

prevented or at least the risk could be lowered by employing medical monitoring, frequent check-ups and glucose regulation[17,18].

Depression

Depression is the most common mental disorder in the general population. One out of ten people will be affected by depression at some point. Today depressive disorder takes the fourth position and it has been estimated that it will take the second position by 2020. The incidence of depression is 9-20%, but more precise criteria have shown that its incidence rate is 3% in males and 4.9% in females[19].

The risk for females to suffer from depression at some point in their lives is almost 20% and for males 10%; among them only 20-25% have a chance of getting cured. The incidence of depressive disorder in females is twice that of males[20]. This difference has been attributed not only to biological aspects and hormonal differences among men and women, but to psychosocial factors and stressful life events (labor, bringing up children) that create an extra burden on women[21].

Depressive disorder can emerge at any point between childhood and old age but half the cases are people aged 20-50 years. On average, depression emerges at the age of 40[19], and seems to be more common in unmarried people, divorced persons and individuals who live in rural areas[22]. Almost half cases of depression go undiagnosed and stay without any treatment, while 10% of depressed patients commit suicide[23,24]. The severity of depression can range from mild to severe. There may be one and only depressive episode, there can be multiple recurring episodes, or it can wind up to be a chronic condition[25]. Nowadays, depression is a treatable condition, yet only 10-25% of all patients receive proper treatment.

According to the WHO, depression will become a major health problem in the developing countries by 2020, affecting more than 25% of the general population; severe depression will become the second most significant cause of death and inability[26].

Negative feelings of sadness, sorrow or frustration are quite common in the course of life, and almost anyone has experienced a feeling of disappointment because of a failure, or sadness after a divorce or any other loss. Sadness can also toughen up and instruct people to cope with the adversities of life. The self-consciousness that derives from negative experiences can lead a person to change, in order to avoid in the future the negative consequences of immature behaviours and actions[27]. If those feelings of sadness linger for more than 2 weeks and affect regular daily activities and functionality regarding work, interpersonal relationships and eating/sleeping habits, then the diagnosis of depressive disorder as defined in DSM-IV-R should be considered[28].

Diabetes Mellitus and Depression

Diabetes, just like any other chronic condition, is accompanied by psychological stress and anxiety, mainly because the patients and their support network (family, friends and spouse) have to adapt to a different way of life and accept the limitations imposed by diabetes. Diabetic persons have also to learn to monitor their glucose levels, calculate and take their insulin doses and deal in a calm way with the occasional hypo- or hyperglucemic attacks.

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Obviously adapting oneself to such conditions calls for flexible thinking and unlimited adaptability to new circumstances. Proper education, willingness to cooperate, combining creativity with imagination and complying with the doctor's recommendations are necessary characteristics. Nevertheless the regulation of diabetes is a complex condition that includes other factors such as the patient's emotional state, since diabetes is a chronic condition that does not have a final cure yet.

Depression is 2 to 3 times more common in diabetic patients, reaching 10-20% of type 1 and 2 diabetics[29,30]. According to several studies, one out of five diabetics has depressive symptoms. Most of the time, these symptoms remain unacknowledged, because diabetes is linked to stressful conditions that trigger feelings of anxiety, frustration and sadness. Sometimes there is an unrealistic feeling that the mere existence of diabetes creates depression[31].

Diabetic persons seem to feel anxiety due to the course of their condition, frustration because of all those things they would like to do but cannot anymore, grief for the potential they think they lost, and sadness for their uncertain future. They also may feel fear because of the difficulties regarding glycemic regulation, anger because they think it is unfair for them to suffer from diabetes, and even guilt because they fail to regulate their diabetes as well as they want to[32]. Moreover, feelings of helplessness, disappointment and hopelessness may also be present. Those reactions are quite normal and are not always present nor are they always severe. But if those feelings are accompanied by classic depressive symptoms, such as loss of enjoyment of life, inability to pursue their interests, negative thoughts about themselves and their future, self-destructive behaviours, disturbed sleeping and eating habits, aggressiveness and anxiety, then clinical depression may be already present[33].

Of course, the fact that depression is more common in diabetics does not mean that diabetes can cause depression and vice versa[34,35]. Specific etiological factors have not been identified yet. It seems that there is a vicious circle where diabetes-related difficulties may lead to depressive symptoms that make diabetes regulation harder because negative behaviours emerge, such as lack of physical activity, smoking, bad eating habits, that lead to more problems and in their turn make depression even more severe[36,37]. Depression can inhibit the most significant factor regarding proper regulation: self-care. It creates a depressive mood, it lowers the patient's energy levels, their functionality and consequently they tend to assess negatively themselves and their condition. People who suffer from depression feel inadequate, think that nothing is important anymore, do not get any satisfaction and are convinced that anything they may try is worthless and their future is negative. The above-mentioned factors discourage the patients and lower their ability to take care of themselves. Depression blocks or diminishes two key factors for efficient problem-solving: one's ability to assess the situation objectively and the ability to stay well-motivated and actively try to solve any given situation. Moreover, depressive patients show direct or indirect self-destructive behaviours. Consequently, suicidal ideation should be thoroughly assessed. Diabetic persons that suffer from depression

cannot take proper care of themselves and regulate glucose levels as instructed, and it has been established that depression is related to poor glycemic regulation[38-40]. It is also possible that patients who fail to regulate their diabetes may suffer from undiagnosed depression that remains without proper treatment[41]. It is not uncommon for depressive signs to be misinterpreted as 'laziness' or signs of 'bad temper', and this way patients not only stay undiagnosed but take the blame from their family, something that makes the vicious circle even worse[42].

Depression is treatable by using a combination of psychotherapy and medical treatment. Nevertheless, it has to be detected early because it can create significant problems to the patient's daily efforts for proper regulation. Depressive diabetic patients may pay no attention to their health, stop taking their treatment properly and develop bad eating habits, just because they do not see any point in complying with their diet and treatment. In such a case, diabetes remains poorly regulated and in the long run acute and chronic complications will emerge.

Discussion

There is a plethora of studies concerning the relationship between diabetes and depression, but there is limited knowledge regarding the way depression can influence the management of diabetes. It was Willis back in 1968 that identified a connection between those two conditions[43]. Most studies confirm that depression can increase the risk for diabetes-related complications, while if depression gets proper treatment glycemic control gets improved too[16,39,44-46]. Some individual studies have found a connection between diabetes and depression, but they do not link glycemic control to depression[38,48]. Only few studies have assessed depression and its influence on glucose and blood pressure regulation; consequently, it is difficult to design a financially efficient strategy against diabetes-related risk factors and complications[39,44,47].

According to interview studies, diabetes was diagnosed before the first depressive symptoms had emerged. The epidemiological study known as Epidemiologic Catchment Area (ECA, 1981), that lasted for 13 years, identified depression as a major risk factor for diabetes[49,50]. It seems that there is a two-way relationship between depression and diabetes, but it remains unclear and more studies are needed for that to be proved.

According to an eight-year long study that employed Zung's self-rating depression scale, patients with moderate or high levels of depressive symptoms (> or = 48 on the SDS, $p < 0.05$), were 2.3 times more likely to develop type 2 diabetes compared to those free of depressive symptoms (< or = 39 on the SDS, $p < 0.05$)[51].

Another study on type 2 diabetic patients assessed depressive symptoms by using both Zung's scale and Beck's Depression Inventory (BDI). According to the findings, patients suffering from diabetic complications had had higher rates of depressive symptoms compared to diabetics without complications, and the BDI scores showed that 74% of diabetic patients with complications had had severe depression as well. Sexual dysfunction was correlated to depressive symptoms in women but not in males[52].

A study on diabetic patients with

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depression showed that patients with severe depression failed to comply with medical instructions, did not follow properly their diet, had poor physical and mental activity, higher needs for treatment and higher treatment costs compared to diabetic patients with less depressive symptoms[53]. A metaanalysis of 42 studies retrieved from MEDLINE and PsycINFO (2001), found that 14.7% of diabetic patients also had had severe depression, while 26% of the population had had depressive symptoms. It also found a correlation between depressive symptoms and diabetic complications and between the treatment of depression and good glycemic control[30].

O' Connor et al.,[54] recently suggested that since diabetic patients have frequent contacts with healthcare settings, it is just easier for their depression to get diagnosed and consequently higher rates of depression have nothing to do with diabetes itself. The authors estimated number of hospital visits as well as if the patients had been diagnosed with diabetes and depression by using the records of 225 000 patients between 1997 and 2003. They compared 2 932 people who were diagnosed with diabetes within that period of time and a group of 14 144 diabetics who had been diagnosed prior to 1997, to two different control groups. The first one was similar regarding age and gender, and the second one was similar concerning age, gender and number of hospital visits. For each patient group, the higher the number of hospital visits the lower the depression diagnosis rates. Diabetic patients with few hospital visits had had 46% more chance of getting diagnosed with depression, while patients with more than ten hospital visits had had the same chance of getting diagnosed with depression as non-diabetics who used to consult their family doctor often.

A previous study in 1997 had shown that diabetic females, specially unmarried and of low educational level, have higher rates of depression; the same applied for diabetics in general with three or more complications[55]. Several studies have linked glycemic regulation to depression. More specifically, diabetic patients with depressive symptoms were found to have higher levels of glycosylated hemoglobin (HbA1c) compared to diabetics without similar symptoms[32,34,37]. Consequently, depression may influence the metabolic control via the neuroendocrine system and also the patients' quality of life[55], and especially patients with type 1 diabetes[56,57]. Some studies have correlated directly depression with the diabetics' poor quality of life, as much as 52%[58].

In another study (2003), where data from the First National Health and Nutrition Examination Survey (NHANES I) and the National Health and Nutrition Examination Epidemiologic Follow-Up Survey (NHEFS) were used, depressive symptoms were assessed by the Four-item Depression subscale of the General Well-Being Survey. The findings showed that the frequency of depression was higher in patients with high depression scores (7.3/1.000 person-years), than patients with medium or low scores (3.4/1.000 person-years and 3.6/1.000 person-years, respectively). Also, the diabetes risk was higher in depressive patients with low educational level[59,60].

Rekleiti et al.,[2] using a sample of Greek diabetic patients (n=164) found high correlation between BMI, central obesity,

female gender, older age and depression. 20% of the sample had had symptoms of moderate depression, while a correlation was found among the duration of the disease (mean 12.96±7.07 years), glycosylated hemoglobin levels and depression severeness[2].

On the other hand, Drøyvold et al., [61] found that diabetic patients are not more prone to depression compared to the general population. The Norwegian team assumed that the relationship between diabetes and depression may be affected by other factors that have traditionally been associated with depression. They used data from the second Nord-Trondelag Health Study where 59 329 persons without diabetes, 223 patients with type 1 diabetes, and 958 patients with type 2 diabetes had been tested for depression using the Hospital Anxiety and Depression Scale (HADS). Depression was more common among diabetics (15.2% in patients with type 1diabetes, 19% in patients with type 2 diabetes and 10.7% in non diabetic persons). Nevertheless, the existence of one or more chronic medical conditions was also more common among diabetics (60.5%, 70% and 31.8% respectively). It was found that diabetic persons without other medical conditions had had the same risk for depression with the general population. Other depression-related factors, such as low educational level, low physical activity and physical inability, showed no difference among diabetics and non-diabetics[62].

Wagner & Abbott [63] found that the treatment of depression in type 2 diabetics may lower the risk for diabetes triggered by biological factors and lifestyle choices. The, mainly obese, participants took part in a diabetes prevention program and it was found that one out of three had had depression and one out of five had been under treatment for depression. Participants who had depression but did not take any treatment had higher insulin resistance compared to those who did not suffer from depression, or their depression was under treatment. Even after those participants had improved their physical activity levels, the differences in insulin resistance levels remained the same.

According to a retrospective study that employed data from the QUEST program, depressive symptoms can influence in a negative way the diabetics' ability to achieve clinical targets such as glucose, lipid and blood pressure regulation[64].

According to another study that included 1801 depressive diabetics over the age of 60, cooperation with healthcare professionals, and proper care and treatment for depression can have positive effects regarding the amelioration of the depressive symptoms, but does not influence glycemic control at all[65].

According to a Greek study) the diabetics' anxiety and depression is linked to poor management of everyday problems, self-destructive behaviour and anhedonia. The study included type 2 diabetics who were under treatment at diabetes clinics in the region of Attiki. The participants had to fill a form that also included the Hospital Anxiety and Depression Scale (HADS). The participants who thought that the management of everyday issues was "too difficult" or even "impossible" had also 2 to 5 times higher anxiety scores and 1.5 to 5 times higher depression scores, compared to those who thought that the management of everyday issues was easy ($p<0.001$). The total

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percentage of individuals who had thought about suicide or had even attempted suicide was as high as 13%, while 23% of the sample claimed to be unhappy. Management of everyday issues was "difficult" for both males (14%) and females (37.9%)[66].

Several studies have shown a strong relationship between depression and diabetic complications, especially neuropathy. Its seems that when diabetic complications worsen, depressive symptoms and sleeping disorders also tend to worsen[16,45,67,68].

Assessment of the patients' difficulties and the creation of a protective framework that seeks to understand the individuals' deeper needs rather than 'invade' their personal space, are extremely significant for the solution of the existing problems, the patients' adaptability, the prevention of complications and the achievement of proper regulation [69].

Conclusions

The strenuous daily efforts for diabetes management can create the opportunity for depression to emerge. Depression, in its turn, prevents the diabetics from taking care of themselves, complying with medical instructions regarding medicines, diet and physical activity, and consequently complications emerge that may compromise the patients' quality of life and increase morbidity.

Tertiary prevention programs can also limit the emergence of complications via early detection and treatment. Interventions should include the patients' training for self-care and glucose regulation, counseling regarding eating habits, treating dyslipidemia and high blood pressure, management of co-existing medical conditions, and regular check-ups for the early diagnosis of diabetic complications. Training the patients aims at providing them with knowledge, and rising awareness regarding prevention and seeking specialized professional help. Continuing education, through group or individual programs, can help with the management of diabetes and can also help with the psychosocial support of patients and families, by improving their quality of life and their mental and emotional state.

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