REVISÃO

Relationship between depression and diabetes *Mellitus*

Relação entre depressão e diabetes Mellitus

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ABSTRACT

Objective

To review studies examining the possible relationship between depression and diabetes *Mellitus*.

Methods

Articles were searched in the following databases: the Latin-American and Caribbean Center on Health Sciences, the Scientific Library Online, Base in Nursing and Pubmed. The search was limited to articles published between January 2000 and October 2010. Search terms included: "diabetes", "depression", "chronic diseases" and "psychiatric disorders".

Results

A total of 21 articles which examined the relationship between diabetes and depression were included in the present paper. There is a bidirectional relationship between these two chronic diseases. Diabetes could lead to depression due its effects on the quality life of patients, its complications and the difficulty in treatment adhesion. Depression could lead to diabetes on account of alterations in glucose transport function and

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increased immunoninflamatory activation, which could contribute to insulin resistance and beta islet cell dysfunction.

Conclusion

There is a bidirectional relation between diabetes and depression and the nature of this relation is still unclear. However, this research contributes to the comprehension of this relation and possible mechanisms involved, since both diseases should be monitored and deserve attention from health professionals.

Keywords: Chronic disease. Depression. Diabetes *Mellitus*.

RESUMO

Objetivo

Revisar estudos que avaliaram a possível existência da relação entre depressão e diabetes Mellitus.

Método

Artigos foram pesquisados nas seguintes bases de dados: Literatura Latino-Americana e do Caribe em Ciências da Saúde, Scientific Electronic Library Online*, Bases de Dados em Enfermagem e Pubmed. A busca foi limitada aos artigos publicados de janeiro de 2000 a outubro de 2010. Os termos de busca utilizados foram "diabetes", "depressão", "doenças crônicas" e "distúrbios psiquiátricos".*

Resultados

Um total de 21 artigos que avaliaram a relação entre diabetes e depressão foi incluído e analisado no presente trabalho. Há uma relação bidirecional entre essas duas doenças crônicas. O diabetes poderia levar à depressão por afetar a qualidade de vida dos pacientes, dadas suas complicações e a dificuldade de adesão ao tratamento. A depressão poderia ocasionar o diabetes devido às alterações na função do transporte de glicose e ao aumento da ativação da resposta imunoinflamatória, o que poderia contribuir para a resistência à insulina e para a disfunção da célula betapancreática.

Conclusão

Existe uma relação bidiretional entre diabetes e depressão, e a natureza dessa relação permanece desconhecida. Esta revisão contribui para a compreensão dessa relação e dos possíveis mecanismos envolvidos, visto que ambas as doenças devem ser monitoradas e merecem atenção dos profissionais da saúde.

Palavras-chave: *Doença crônica. Depressão. Diabetes Mellitus.*

INTRODUCTION

Diabetes *Mellitus* (DM) is defined as a metabolic disorder, characterized by chronic hyperglycemia resulting from partial or full insulin deficiency or its failure. When developing DM, the person has abnormalities related to glucose, lipid and protein metabolism[1,2]. This pathology has been classified by different organizations as the epidemic of the century, affecting thousands of patients all over the world, being recognized as a public health problem in several countries[3].

According to the *Sociedade Brasileira de Diabetes*[4], diabetes has high rates of morbidity and mortality, being one of the main causes of mortality, renal failure, hind limb amputations, blindness and heart disease.

The World Health Organization (WHO) shows that the prevalence of diabetes varies between countries. In 2006, there were approximately 171 million people affected by this disease, and it is on the increase: it is estimated that, in 2030, this number will double. DM occurs in all countries, but is more

common (particularly type 2) in developed countries. This increase is due to the trend towards urbanization and lifestyle changes[5]. In Brazil, more than 6 million people have confirmed diagnosis[6]. The average rate in the adult population is 5.2%[6,7].

From all cases of diabetes, 90% are type 2, 5%-10% are type 1, while only 2% are another type or associated to other syndromes. Gestational diabetes, a transient condition during pregnancy, occurs in approximately 2% to 3% of gestations[8]. Type 1 Diabetes (T1D) is characterized by the destruction of pancreatic beta cells[9], resulting from an interaction between genetic predisposition and environmental factors, such as exposure to toxins early in life, lack of vitamin and stress[10-14]. The role of enterovirus infections has also been reported[15]. Type 2 Diabetes (T2D) is caused by a defect in the secretion and action of insulin (insulin resistance). Around 80% of patients present overweight and obesity and, even those with normal body weight, may have a higher predominance of abdominal fat[6]. This type of diabetes correlates with genetic predisposition, lifestyle and other environmental factors[16,17]. In uncontrolled cases, a progressive pancreatic beta cells failure might occur, leading to insulin dependence. This type of diabetes presents strong genetic predisposition[18]. Recent evidence shows that T2D does not present a favorable prognosis, resulting in an enormous physical, psychological, economical and social impact.

The diabetic syndrome might be related to one of the most common psychiatric disorders among individuals, depression, which nowadays affects the majority of the population. Depression may act as a risk factor for the development of diabetes, or vice versa, and besides making the symptoms worse, it interferes with the patient's self-care when it is treated inappropriately[18].

Depression is a common, chronic and recurrent medical condition. It is frequently associated with functional disability and a compromising of physical health. Depressed patients present limitations in their activities and welfare, in addition to greater use of health services[19]. Risk factors associated with depression include family history, adversity in childhood, aspects related to personality, social isolation and stressful experiences[20]. Depression might be inherited and it shows a tendency towards abnormal biochemical activity in some regions of the brain. Some people might develop the disease because of this abnormal activity. Most cases of depression seem to be genetically transmitted and chemically produced[21].

According to the WHO, in the next two decades, there will be a change in health necessities of the population, due to the fact that diseases such as depression are rapidly substituting traditional problems of infectious diseases and malnutrition[22]. Depression is a constant and serious mood disorder which occurs in all ages. Rates may increase among young and old people. It is not clear why depression is becoming more and more frequent this century[21].

Considering these two important diseases, it is postulated that there is a relationship between them, since an individual with DM changes his daily routine and consequently is exposed to important risk factors for possible depression. Depression has a significant impact making several other diseases worse and may predispose the individual to other pathologies[23].

Therefore, it is necessary to understand the relationship between diabetes and depression so that the control and prevention of diabetes are effective, and to consider depression as a relevant factor in this process. Nevertheless, this study aims to identify the existing relationship between diabetes mellitus and depression. Thus, the result of this research will contribute to a better understanding about the subject, providing support to better assist these patients.

METHODS

In order to identify relevant literature, the databases searched included the Latin-American and Caribbean Center on Health Sciences (LILACS), the Scientific Library Online (SciELO), Base in Nursing (BDENF) and Pubmed (from January 2000 to October 2010). Search terms included: "diabetes",

"depression", "chronic diseases" and "psychiatric disorders". The studies were eligible for inclusion if they were available in the databases and in Portuguese or English. Since no methodology was considered, quantitative and qualitative methodologies were included, as well as case reports and literature reviews.

RESULTS

A total of 21 articles were included in the present paper (see Table 1 for a summary of the articles).

DISCUSSION

Depression and diabetes are among the most prevalent diseases in their respective fields, metabolism and psychiatry, all over the world. However, there is evidence that diabetic patients have an increased risk of developing depression, although a bidirectional relation might also exist[24]. Depression in a patient with diabetes tends to compromise life quality, affecting physical health, psychological health and social relationships[29].

The presence of depression in diabetic patients has been associated with an amplification

Table 1. Summary of studies reviewed published from 2000 to 2010 regarding diabetes and depression and their respective highlights

Study	Highlights
Fráguas *et al*.[18]	Some medicine used in the treatment of depression, especially those with greater noradrenergic action, may increase blood glucose levels.
Moreira *et al*.[23]	The treatment of depression could help in the control of glycaemia, reducing the risk of chronic complications of diabetes.
Castillo-Quan *et al*.[24]	Diabetic patients have increased risk of developing depression due to neurochemical mechanisms.
Nascimento *et al*.[25]	A stressor agent may act in the hypothalamic-pituitary-adrenal axis, thus increasing the synthesis and release of cortisol, (a hypoglycemic hormone), which injuries the metabolic control in T2D, predisposing the individual to depression.
Raval *et al*.[26]	Hormonal alterations, mainly hypercortisolemia, besides the increase of the immunoinflamatory response activation, could explain the greater risk of diabetes in patients with depression.
Moreira *et al*.[27]	Diabetic patients with diabetic distal polyneuropathy present more depressive symptoms than patients who do not have the disease.
Nascimento *et al*.[28]	Individuals with T2D with high levels of education and low income are more susceptible to depression.
Eren *et al*.[29]	The presence of depression in patients with T2D affects life quality of these patients, evidencing the importance of the treatment of depression in this context.
Péres *et al*.[30]	Women's behavior after the diagnosis of diabetes associated with feelings and emotional reactions which interfere with treatment adherence.
Papelbaum *et al*.[31]	Evidence of increase of bulimia nervosa and subclinical eating disorders among women with diabetes.
Carrijo & Dela Coleta[32]	Depressive symptoms influence diabetes treatment adhesion.
Rocha & Bezerra[33]	Higher rates of metabolic disorders are observed in patients with psychiatric disorders than in the general population.
Teng *et al*.[34]	Association of depression to several diseases, such as cardiovascular disease, endocrinological conditions and so forth.
Marcelino & Carvalho[35]	The bidirectional relationship between diabetes and emotional disorders in children. Some cases of diabetes have been controlled without medication, only with the treatment of depression.
Katon *et al*.[36]	Diabetic complications associated with depression was more prevalent in men and among individuals under the age of 65.
Ciechanowski *et al*.[37]	Depression symptoms were more prevalent in diabetic patients with poorer physical functioning and less adherence to exercise regimes and diet.
Martins *et al*.[38]	Depression is directly associated with the control of glycaemia and other factors, such as obesity and sedentarism.
De Groot *et al*.[39]	A significant association of depression with a variety of diabetes complications.
Anderson *et al*.[40]	Diabetes doubles the odds of comorbid depression.
Lustman *et al*.[41]	Depression is mainly associated with poor control of glycaemia in diabetic patients and it is important to identify the directional nature of this relationship.
Ricco *et al*.[42]	Higher risk of symptoms of depression in patients with chronic diseases, such as hepatitis C and DM.

Note: T2D: Type 2 Diabetes; DM: Diabetes *Mellitus.*

of symptoms, in other words, those with depression presented more symptoms than those who did not have the disease, even when a statistical adjustment was made for diabetes severity[37].

A 1.3 times greater risk of developing diabetes in patients with moderate or severe symptoms of depression has been reported. A risk of 2.2 was found in patients with clinical depression. A possible explanation would refer to the hyperactivation of the Hypothalamic-Pituitary-Adrenal (HPA) axis related to depression[23]. High levels of catecholamines would be associated with an increase of glucose levels and glucose intolerance. Therefore, there are no studies which evaluate the impact of treatment of depression in the incidence of DM.

There are two factors which seem to be correlated with depression in diabetic patients: the acceptance of the disease and the ability of the patient in handling the changes imposed in some aspects of daily life. The difficulty in adapting to the disease might be associated with an increase of depressive symptoms, having a negative impact on these individuals' daily lives. The functional impediments would have an even greater impact on their lives[23].

Some studies have shown an association between diabetes and depression, demonstrating that depression might be related with hypoglycemia and complications related to diabetes[39-41]. It has been proposed that biochemical changes associated with depression or its treatment may have a domino effect that results in diabetes[43]. Fráguas *et al*.[18] reported that tryciclic antidepressant, especially those with more noradrenergic profile, and monoamino oxidase inhibitors are associated with worsening of glycaemic control[18].

Only one third of patients with diabetes suffering from depression are diagnosed properly, and thus, it is important to highlight that correct diagnosis and treatment leads to remission of depression and decreased risks of morbidity and mortality[44,45].

Young patients with diabetes present greater symptoms of depression which can be explained by the difficulty of adjustment, related to the diagnosis of a chronic disease in early life[23]. According to Nascimento *et al*.[28], patients with diabetes, particularly females, those with less education and with a low income, present a greater risk of developing depression. However, diabetic complications associated with depression were more prevalent in men in a study conducted by Katon *et al*.[36].

Some of the explanations for a link between diabetes and depression include: alterations in monoamines (serotonin and noradrenalin) which increase cortisol by the HPA; and trophic agents as a neurotrophic factor derived from the brain, through the glycogen sinthase kinase 3 inhibition, which constitute some of abnormalities documented in diabetic patients and animal models. Furthermore, psycho emotional factors should be considered, since they might be connected with the relationship between depression and diabetes[24].

Influence of environmental factors on depression and diabetes

It has been suggested that the manifestation of psychotic symptoms could be due to an interaction of environmental and genetic factors, where a high number of genes of susceptibility, that individually would cause only mild effects, but when matched could lead to an interaction with environmental factors, consequently leading to psychotic effects[40]. However, these genes have not yet been identified. Nevertheless, the hypothesis that metabolic syndrome components and psychiatric diseases genes may have a common identity or even an inference in their actions, cannot be denied[26].

Influence of diagnosis and treatment of diabetes on the development of depression

A good adhesion to treatment, along with advances in medicine, might be considered categorically as one of the most efficient means to

mitigate, or even cure the pathology, along with an indicator of good health. Adhering to treatment means to accept and properly follow the therapeutic modality proposed by the health professional. Thus, several factors influence the adhesion to treatment: characteristics of the therapy, the private conditions of the patient, relations with the medical team, psychosocial and socioeconomic variables, and so forth[32].

Multidisciplinarity has become more and more frequent in studies and health treatments. The presence of depressive symptoms has a negative impact on the treatment of patients with chronic diseases. Thus, the psychosocial variables might have a significant influence on cognitive aspects related with the way the patient reacts to his treatment[37,41,44]. Chronic diseases are seen as a long term stress factor which affects not only the patient, but also their relatives[44]. It is believed that around 50% of chronic disease carriers do not follow appropriate or sufficient commitment to treatment[46].

Diabetes is a chronic disease which affects the quality of life of patients and also gives rise to adhesion problems. Medical treatment does not come without its own difficulties since in order to control this disease and avoid all possible complications, it is necessary to carry out exams, and commit to diet, physical exercise, stress control and so on, which is dependent on the patient alone[47]. A multidisciplinary approach is needed when dealing with this disease.

It is important to highlight that diabetic patients constitute a highly diverse group, which includes members of both sexes with different health statuses and from different social strata. Diabetes may appear at any age and never disappears after its first appearance. Regarding these aspects, the diabetic patient might experience distinct psychological manifestations which favor an emotional imbalance, leading to a strict adhesion to treatment, along with other psychological and negative psychosocial manifestations[32]. Patients suffering from DM need to change their lifestyles and to adhere to therapy, as well as regular insulin applications and daily glucose monitoring.

Diabetes induces alterations in several systems, making these patients more susceptible to complications such as blindness, chronic renal failure, heart disease, and so on, which cause considerable difficulty in carrying out common activities, affecting mood, and thus leading to depression. Patients with chronic diseases and depression have a greater risk of not adhering to medical recommendations[48].

Some researchers report that, in recent years, the number of studies which correlate DM with depression have increased, so there are new conclusions: repetitive treatments can overload patients; the duration of the disease generates stress; complications may affect life quality; and DM and depression are part of a group of common metabolic disorders or linked to each other. Diabetic patients with depression present a higher risk for obesity, while the lower they are in terms of economic and educational levels the higher their vulnerability to psychosocial and financial stressors[34].

Finally, patients with diabetes-depression comorbidity present worse glucose control and a higher incidence of complications resulting from diabetes, such as retinopathy, neuropathy, sexual dysfunction, neuropathy and macrovascular complications[34].

Some evidence suggest that alterations in glucose transport in specific regions of the brain could occur in diabetic patients, favoring the emergence of depression, and that hormonal alterations, mainly hypercortisolemia, along with the increase of immune inflammatory activation, could explain the higher risk of depression in diabetic patients[49].

Limitations of this study include the absence of an analysis of quantitative data of the literature included in this analysis. However, our aim was to report and to describe the existence of the relationship between depression and diabetes.

CONCLUSION

As reviewed in this study, there is a clear relationship between diabetes and depression. The

biochemical and physiological changes associated with diabetes, and psychosocial burden of a chronic disease has been evidenced in some studies. The risk of diabetic patients developing depression results mainly from changes in lifestyle, the daily application of insulin and complications related to the disease. Depression gives rise to neurochemical and hormonal changes that cause disturbances in blood glucose levels. Diabetes *Mellitus* has neurochemical effects on serotonergic, noradrenergic and dopamine central systems, which could lead to a decrease in monoamine function similar to what occurs in depression. Also, some medicine used in the treatment of depression may lead to hyperglycemia, triggering diabetes. Nevertheless, this study presented the bidirectional relation between these two important chronic diseases. Although the exact nature of this relation is still unclear, it is important to be aware of this relation in order to better assist patients.

CONTRIBUTORS

T DALZOCHIO helped to literature review, analyze and discussion about the covered theme. L BONHO helped to literarture review. L FEKSA and DB BERLESE helped to review of manuscript.

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