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The Impact of Anxiety and Depression on the Pediatric Patients with Diabetes

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Abstract

Diabetes mellitus represents a vast pathology which attestation is known since ancient times and research made in the recent years reveals increasingly clear data on the connection between diabetes and psychiatric disorders. Diabetes can cause psychiatric disorders such as anxiety, depression, acute stress response and adjustment disorders, as well as organic personality disorders and/or affectivity disorders. There is an increase in diabetic patients worldwide and in the same time for the pediatric cases with diabetes. Moreover, there is an association between the development of anxiety and depression symptoms in patients with diabetic comorbidity and the association of these three entities represents an interesting subject in the medical world. The main purpose of this study is to deepen the knowledge about the association of three diseases in children, in order to establish a working algorithm applicable in current clinical practice. We were able to identify the severity of anxiety and depressive symptoms in patients with diabetes mellitus insulin dependent and no other psychiatric pathologies diagnosed before the study by applying the Hamilton A questionnaire, Beck Depression Inventory and Children's Depression Inventory. There were analyzed correlations between their scale's scores and the values of our patient's glycemia, glycosylated hemoglobin, number of insulin doses per day and the calories consumed per day. This study makes an important contribution highlighting the psychological aspects in the context of medical conditions, referring to the therapeutic relationship and approaching of the pediatric patient in a bio-psycho-social context, recognizing the complexity of the factors that contribute to a medical success in the pediatric field related to the type of special relationship in which several persons are involved incuding the relatives of the patients. Given the particularities of the individual with normal mental development during adolescence, recognized as a period of psychobiological crisis, it is important to realise a pattern of therapeutic interaction with this category of patients who associates anxiety- depression- diabetes.

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1. Introduction

Diabetes is the fifth leading cause of death worldwide; the presence of the disease generates a reducing of life expectancy by an average of 12-15 years. The statistical data is influenced by the age at which the disease made its onset. About 80% of patients die due to cardiovascular events, diabetes being an independent risk factor for this disease, increasing the risk of death 2-4 times more than in non-diabetic patients (Manuel & Schultz, 2004). In developed countries, multidisciplinary research have concluded that diabetes is the main cause of blindness (the risk of blindness of a diabetic patient is about 10 times higher), amputations of non-traumatic origin (due to trailing ulcers and painful syndrome), but also of chronic renal failure, through the presence and progression of diabetic nephropathy (Pickup & Williams, 2003). The association of diabetes with psychiatric disorders such as anxiety and depression represents nowadays a major public health problem (Agrawal et al., 2016) related not only to the medical consequences (Bai et al.,2017; Melin et al.,2017; Mutlu et al., 2015) as well as those of a social and psychosomatic type (Martino et al., 2020; Munkácsi et al., 2018; Settineri, 2019; Settineri et al., 2019a, 2019b, 2019c). If we refer to the pediatric population (Agrawal et al., 2016; Khandelwal et al., 2016), the prognosis is negative because this comorbidity, encountered more and more frequently, brings significant individual and social damage by decreasing the capacity for a normal social insertion, the capacity for developing relationships, long term education and training (Baykara et al., 2012; Beverly et al., 2019) as well as the development of professional activity in adult life (Pace & Muzi, 2019; Marchini et al., 2018; Rosa et al., 2019; Kafali et al., 2020; Settineri et al., 2018). Although apparently it is only a medical problem, the sum of these aspects has an important social projection (Williams, Sharpe, & Mullan, 2014; Sancanuto et al., 2014) reason for which it is necessary to decipher more and more clearly through the in-depth study of the strictly medical aspects with the psychological ones (Duru, Civilibal, & Elevli, 2016; Pop-Jordanova & Gucev, 2015) in order to find optimal solutions for recovery of this category of patients and their favorable evolution

in the future (Buschur, Glick, & Kamboj 2017; Felicio et al., 2015; Lopez- Bastida et al., 2019; Khemakhem et al., 2020; Martino et al., 2020, Rasmussen et al., 2020).

Numerous studies over the years have also shown that patients with known diabetes are twice as likely to develop psychiatric conditions such as anxiety and depression compared to non-diabetics (Rose et al., 1983).

Patients with diabetes mellitus type 1 (DMt1) need a different and somewhat more complicated treatment regimen compared to diabetes mellitus type 2 (DMt2). They need frequent blood glucose monitoring, adjusting insulin doses, diet and physical activity accordingly. The age at which DMt1 debuts is known to be much more recent than for DMt2. In this case it can be seen that the close chronological relationship between DMt1 and the debut of depression is striking, the diagnosis of DMt1 and the need to apply the treatment regimen occur at a time when the individual has an increased vulnerability to depression (Moulton, Pickup, & Ismail, 2015). Children and adolescents with diabetes are prone to depression two to three times higher than those without diabetes (Grey, Whittemore, & Tamborlane, 2002). Low glycemic control in pediatric DMt1 is associated with both depression and low socioeconomic status, and the chances of depression in these patients increase as glycemic control worsens (Hassan et al., 2006).

Stress, manifested through anxiety, is an important factor in cases where blood glucose cannot be kept under control despite medical treatment (Dobrica et al., 2019; Hainarosie et al., 2019). Therefore, in recent years, numerous studies were conducted on the levels of involvement of mental health problems suffered by diabetic patients, as well as the factors associated with mental health problems (Ozkan, 1995; Suceveanu et al., 2018; Zugravu et al., 2012).

A recent epidemiological study, conducted on a population of 90,686 participants, found that depression was more common in people with diabetes, regardless of whether they had known about their diabetic estate. The same study showed that anxiety was more common only in participants who were aware of their diabetes. (Meurs et al., 2016).

One possible explanation could be that the psychological burden of being ill can play an important role in triggering anxiety and depression. However, the fact that in patients with previously undiagnosed diabetes, depression had a higher prevalence and may be due to an unfavorable lifestyle, such as physical inactivity, unhealthy diet or a stressful lifestyle. Severe hypoglycemia in patients with DMt2 and without antidepressant treatment was positively associated with the severity of depressive symptoms, independent of glycemic control, insulin therapy, lifestyle factors, and diabetic complications (Kikuchi et al., 2015).

The Beck Depression Inventory (BDI / Beck scale) is a prototype of self-rating scales. The BDI scale was designed by Beck with his collaborators in 1961. It was designed as a questionnaire to assess the severity of depressive symptoms, consisting of 21 items, each corresponding to a question whose answer is quantified in the form of four degrees of severity (0 being absent and 3 very severe, maximum 63 points), minimal range = 0–13, mild depression = 14–19, moderate depression = 20–28, and severe depression = 29–63 (Beck et al., 1981).

The Children's Depression Inventory was designed after Beck Depression Inventory for children with ages between 7-17 years old and included 27 items evaluating negative mood, interpersonal problems, ineffectiveness, anhedonia and negative self esteem (19-20 generally accepted, 20-36 mild symptoms and more than 36- severe depression) (Kovacs, 1992).

The Hamilton Anxiety Rating Scale is one of the first instruments to measure anxiety and was developed in 1959 by Hamilton to be used to assess the severity of anxiety neurosis. The scale can be used both to highlight the symptoms of anxiety and to assess their severity (Hamilton, 2000). It consists of 14 items, each item is evaluated using scores from 0 to 4, and the total score is between 0 to 56, where <17 indicates mild severity, 18-24 mild to moderate severity and 25-30 moderate to severe symptoms of anxiety. The HAM-A is in the public domain. (Borkovec & Costello, 1993; Maier et al., 1993).

The validity and reliability of these scales were tested during the time though many studies, this one being the main reason of chosing them for developing and completing the study (Clark et al, 1994; Knight, Hensley, & Waters, 1988; Mayer et al., 1988; Toledano-Toledano, 2018)

1.1 The current study

This study joins a significant number of other studies that address an increasingly common pathology and unfortunately, with major long-term medical and social consequences. An aspect of maximum interest of this pathology refers to the patient's life quality considering the relationship to two factors, namely, longer life expectancy in the pediatric population and complications of comorbidities, factors that are interrelated.

The novelty of this study is the possibility to provide a working algorithm to facilitate the early establishment of comorbid condition in clinical practice, being known that the type of therapeutic relationship in pediatrics is particular and one of the most difficult in clinical practice if we refer to each of the two types of pathologies: metabolic and psychiatric. In addition, the screening methods are considered among the most effective, both from a clinical and cost perspective in the medical system, according to literature.

The aim of this study was to emphasize the importance of having a rigorous screening in population with diabetes mellitus for psychiatric symptoms before their somatic and psychiatric manifestations. The working hypothesis are based on the corroboration of the data obtained after the laboratory investigations and the anamnesis as well as after the completion of the questionnaires for detecting the symptoms of anxiety and depression in children and adolescents with diabetes.

2. Material and methods

2.1 Participants

We conducted a study on one hundred patients with insulin-dependent diabetes mellitus, 50-50 female to men, aged between 10 to 18 years old. The study extended on a period of 3 years. To centralize the data, there were studied the patient's observation files and they were given Hamilton A questionnaire, Beck Depression Inventory and Children's depression inventory for those below 10 years old. Patient files were prepared for each studied patient in which there were noted socio-demographic characteristics, clinical and paraclinical data. The questionnaires for anxiety and depression were completed and also attached to the personal patient's file. The evaluation of the parameters was performed either at the time of hospitalization or at the time of presentation in the specialized outpatient clinic.

2.2. Ethical Statements

The subsequent research was carried out under the conditions of signing an informed consent, obtained from the parents / legal guardians of the patients, taking into account the legislation in force of the World Health Organization and the European Union regarding the research on patients in the medical field, and the study was approved and supervised by the Ethics Committee of the hospital corresponding to the study group and respecting the rules of clinical studies on human subjects (Declaration of Helsinki).

2.3 Instrument and procedures

The statistical data were analyzed using IBM SPSS Statistics 23 and Microsoft Excel.

For the patients included in the study, the following factors were analysed: blood glucose value, glycosylated hemoglobin (HbA1c) value, number of calories consumed per day, number of insulin doses per day, the existence of associated comorbidities, as well as the degree of anxiety and depression depending on the answers to the anxiety questionnaires (Hamilton A) and depression (Beck, CDI), questionnaires that were completed with the help and consent of the legal guardians or parents of the patients included in the study.

From a clinical point of view, there have been followed the family history, personal physiological and pathological history, backgrounds, training level, financial situation, number of calories consumed per day, number of doses of insulin to be taken daily by patients with insulin-dependent diabetes, the medication received at the time of hospitalization.

As work tools, there were used: the informed consent of the patient, patient observation sheets, individual questionnaire, sampling lists, summary tables and blood glucose tests with strips. All patients enrolled in the study completed the individual questionnaire and the scales that were used to quantify the severity of psychiatric pathology if existent. The scales used in the study were Beck Depression Inventory (BDI / Beck scale), Children's Depression Inventory (CDI) and the Hamilton Anxiety Scale (HAM-A).

2.4 Inclusion and exclusion criteria

Criteria for inclusion in the study: age between 10 and 18 years, patients with diabetes, signed informed consent of their legal guardians, completion of the depression and anxiety questionnaires.

Exclusion criteria from the study: age over 18 years, patients without discernment, undiagnosed patients with diabetes, patients whose legal guardians refused to sign the informed consent.

2.5 Limits of the research:

- the small number of patients, but this aspect, however, does not harm the veracity of the results respecting the numerical criteria imposed, from the perspective of statistical processing;
- the subjectivism determined by the fact that some of the patients belong to the pediatric sample, the answers being provided in this case by the parents or legal guardians.

3. Results

Following the study of patients with insulin-dependent diabetes mellitus, aged between 10 and 18 years, there were determined correlations between the degrees of anxiety and depression and diabetes in patients who participated and completed the questionnaires for anxiety and depression (accompanied by parents or their legal guardians), who were given blood glucose tests, HbA1c and who provided data on lifestyle, number of calories consumed per day and number of insulin doses to be taken in a day.

Among the patients in the study, the proportion by sex was 50-50 male-female, the vast majority in urban areas (45 vs. 55 patients). From the point of view of the caloric regime, 61 patients consumed between 2000-2500 kcal per day, 22 between 1500-2000kcal, 11 patients between 1000-1500kcal and 6 patients over 2500kcal. The HbA1c values detected in pediatric patients, with the age between 10-18 years, had an average of 12.91%, with an extreme minimum of 6.79% and a maximum of 25.68%. For glycemic values, the minimum value detected with the help of the blood glucose test was of 51 mg / dL, and the maximum reaching the threshold of 947.90 mg / dL. The average obtained in this case is 339.53 mg / dL.

Table 1. Number of Insulin Doses Administered per Day

Dose frequency per day	***No.of patients***	***Valid percentage (%)***
0	2	2
1	3	3
3	46	46
4	47	47
6	2	2
	100	

Table 2. Anxiety Diagnosed by Applying Questions from the HAM-A Scale

Degree of anxiety	***Patient frequency***	***Valid percentage (%)***
None	37	37
Mild	51	51
Moderate	12	12

Out of 100 patients to whom the Beck and HAM-A questionnaires were applied, anxiety (Table 2) can be quantified as follows:

- N = 51 is the number of patients diagnosed with mild anxiety;
- 12 of the patients surveyed had moderate anxiety;
- 37 patients did not show anxiety.

The psychiatric pathology pursued in this group also includes depression. The share of patients who have been diagnosed with this condition is different from that of patients who have had the HAM-A scale applied.

Thus, the vast majority of children over 10 years old do not show (according to the Beck and CDI questionnaires) any signs or symptoms specific to depression (n = 72). On the other

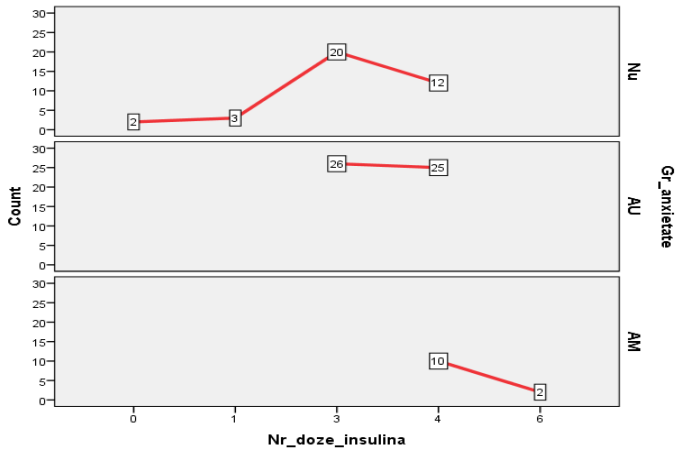
hand, mild depression can be observed in n = 21 patients, and the average depression in an even lower number, in only 7 of the respondents (table 3.)

Table 3. *Depression Diagnosed by Applying BECK Scale Questions*

Degree of depression	***Patient frequency***	***Valid percentage (%)***
None	72	72
Mild	21	21
Moderate	0	0

The quantification of the degree of anxiety according to the number of insulin doses is shown in the figure below (Figure 1). As can be seen, the highest proportion of high insulin doses was given to patients who were diagnosed with mild to moderate anxiety. Thus, an intensive insulin regimen (4 doses / day) administered to 10 patients with moderate anxiety, 25 diagnosed with mild anxiety and 12 patients who do not associate psychiatric symptoms. There are 46 patients in the 3 times per day insulin regimen, of whom 26 were diagnosed with mild anxiety and 20 did not show relevant results after completing the HAM-A questionnaire.

Figure 1. Degree of Anxiety Depending on the Number of Insulin Doses



As a statement, in the case of patients whose psyche was affected, the results obtained in questionnaires is directing the diagnosis to that of the association of psychiatric symptoms, there were necessary to apply intensive insulin regimens for proper control of diabetes (3, 4 and 6 doses per day). At the same time, for the patients who completed BECK questionnaires to quantify the degree of depression (Figure 2), signs and symptoms of moderate and mild depression were detected for the patients with increased need for insulin doses (the vast majority being reported by patients who follow a 4 dose per day regimen):

- 7 patients with 3 doses per day of insulin diagnosed with mild depression;

- Of the 47 patients receiving treatment with 4 doses per day, 14 have mild depression and 5 moderate depression;
- Only 2 patients who have been diagnosed with moderate depression receive treatment with 6 doses of insulin per day.

Figure 2. Degree of Depression Depending on the Number of Insulin Doses

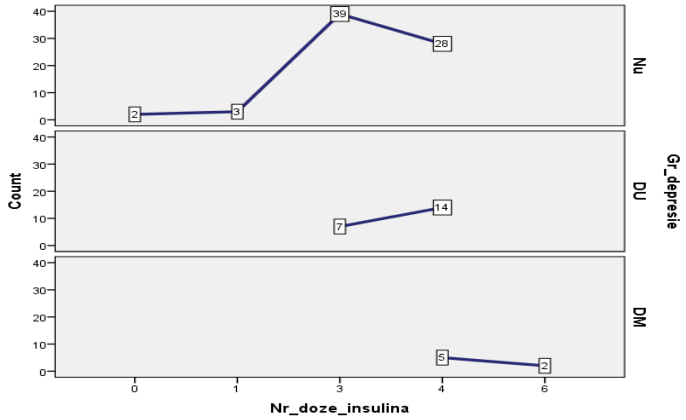


Table 4. Pearson Correlations between Number of Insulin Doses per Day, Number of Calories Consumed per Day, Anxiety and Depression Degrees

		Anxiety degree	Depression degree
Number of insulin doses/ day	Pearson Correlation	,454**	,404**
	Sig. (2-tailed)	0,000	0,000
	N	100	100
Calories consumed per day	Pearson Correlation	-0,192	-,341**
	Sig. (2-tailed)	0,056	0,001
	N	100	100
Anxiety degree	Pearson Correlation	1	,599**
	Sig. (2-tailed)		0,000
	N	100	100
Depression degree	Pearson Correlation	,599**	1
	Sig. (2-tailed)	0,000	
	N	100	100

**. Correlation is significant at the 0.01 level (2-tailed).

There are strong correlations for the detected values of the Pearson index of 0.01. These are statistically significant for the following:

- Number of insulin doses and groups of glucose values, glycated hemoglobin value, degree of anxiety and degree of depression

- Glucose value and glycated hemoglobin value
- Calories corresponding to the regimens administered to patients and the degree of depression
- Degree of anxiety and degree of depression.

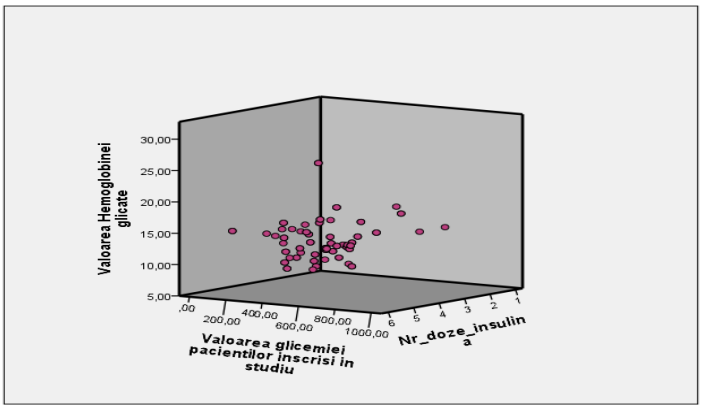
Figure 3 is a 3D scatter plot that shows the relationship between 3 scalar variables (continuous variables). As can be seen from the analysis of the figure, as a conclusion of the interaction of these 3 variables it can be stated that:

• The highest share of patients has declared HbA1C values between 6.5 and 20%, respectively, with an average of 12.91 and a Std Dev of +/- 3.30

• Their glycemic values are mostly in the range of 250 mg / dL - 650 mg / dL, with an average of 339.53 mg / dL , Std. Dev = 185.48 and extremes located at 51mg / dL, respectively 947.90 mg / dL

• The average number of insulin doses given is 3.41, most doses being 3 (n = 46) and 4 doses (n = 47) per day.

Figure 3. HbA1c Values, Patients' blood Glucose Levels, No. of Insulin Doses



4. Discussions

Contrary to our study, Zambanini, Newson, Maisey, and Feher found in their 1999 study that no significant correlation between HbA1c, number of injections per day and anxiety existed, but there were some similarities in an unselected group of diabetic patients a generalized anxiety related to insulin injection (Zambanini et al., 1999).

It is recognized and increasingly scientifically fundamented, in the context of EBM (Evidence Based Medicine), the link between chronic diseases, type II diabetes, in this case and psychiatric disorders, anxiety and depression in the context of this study (Conversano, 2019).

Morover, in Strandberg's 2014 study, there have been concluded that in young adults with DMt1, glycemic control was not significantly associated with depression, anxiety, and general well-being, but was significantly associated with diabetes-specific emotional distress, especially in terms of regarding the treatment regimen. (Strandberg et al., 2014). According to a 2012 review by Johnson and colleagues, they found data similar to the present study: patients with high levels of glycated hemoglobin have more symptoms of depression (Johnson et al., 2013).

The present study falls into the category of those who address the biopsychosocial context of the patient with chronic comorbid disease with anxiety and depression, emphasizing the importance of psychological factors on the evolution of chronic disease (Turk & Okifuji, 2002).

Another interesting aspect refers to the connection between the quality of a patients' life with metabolic diseases, reffering to the restrictions imposed by a certain type of diet and the psychological consequences that implicitly affect the psychological well-being of patients and their quality of life in general (Doneddu et al., 2020; Guicciardi et al., 2019; Martino et al., 2019; Vicario et al., 2020).

The impact of the association between diabetes, anxiety and depression involves a particular implication, especially in the pediatric population, mostly in the educational aspect, both in terms of nutrition but also referring to the mental hygiene of children and adolescents, with repercussions in adulthood (Merlo, 2019a, 2019b). Furthermore, concerning the comorbidities studied in this paper, another aspect of interest refers to the particular therapeutic relationship established between the doctor and the patient with psychiatric illness, being accepted that a positive metabolic evolution is dependent on a good mental functioning (Caputo, 2013).

The relationship between the patient's cognitive status in the case of metabolic disorders and the cognitive status in the context of anxiety and depression is an aspect of interest in this study and also a topic of interest in other studies published in the literature(Guicciardi et al., 2019).

Given the particularities of the individual with typical mental development during adolescence, recognized as a period of psychobiological crisis, it is important to realise a pattern of therapeutic interaction with this category of patients, pattern adapted to the comorbidities mentioned in the study (Di Giuseppe et al., 2019; Gugliandolo et al., 2020; Inguglia, 2020).

None of the less, another important studied aspect is that of the defense mechanisms triggered by the coexistence of cancer associated with anxiety, depression and diabetes (Di Giuseppe et al., 2020). Anxiety and depression are considered as important factors in the

evolution of various diseases, both in children and adults, in various pathologies, from aesthetic medicine (Ardeleanu, Dobre, & Georgescu, 2015; Ardeleanu et al., 2017; Jecan et al., 2017), to acute or chronic non-lethal diseases (Ardeleanu et al., 2010, 2013; Stoian et al., 2017, 2018a, 2018b) and up to diseases with a reserved prognosis (Ardeleanu, Francu, & Georgescu, 2014; Ardeleanu et al., 2014). Thus, a high morale can help a lot to increase self-confidence and a favorable evolution of the disease, or on the contrary depression and especially anxiety can negatively influence the evolution of many diseases, including diabetes.

In addition, the study may be a basis for other studies to enlarge the approach from an individual psycho-medical perspective at the social level, by the current and long-term costs and also by the complexity of managing such a category of patients. The design of the study also offers the possibility to continue the research in the direction of establishing behavioral patterns in various stages of the child's development, with reference to the small school, the preadolescent and the adolescent. This aspect is important to emphasize because with the transition from one stage of evolution to another, the child faces a series of factors determined by the development of social relations, the adaption of new behaviors and last but not least his biological and mental transformation, as an individual.

Another novelty of the study refers to joining the two perspectives, medical and psychological that complement each other, thus outlining the profile of a pediatric patient with a type of comorbidity that profoundly affects the individual and family status of the patient. It is well-known that this category of children and their families face medical problems, which affect both internal and extra-family relationships. This is the reason why in many situations the evolution and prognosis of these patients are not favorable, complications are common and the relationship with the medical and educational system is not as good as it is expected to be.

Consequently, this study is about a morbidity with a strict reference to the medical aspect, but it is also related to the psychological aspect determined by the medical condition which is interconditioned, requiring a multidisciplinary, complex and permanent approach (Dimitriu et al., 2020; Mokhort & Navmenova, 2015; Motovilin et al., 2012).

5. Conclusions

According to the scores, obtained after the application of the Hamilton A questionnaire, we can state that, in the case of patients whose psyche has been affected, the results obtained drives the diagnosis to mild and moderate anxiety due to intensive insulin regimens for proper control of diabetes (3, 4 doses per day) and the low-calorie diet, as well as a poorly controlled glycemic level.

When applying the depression scales, similar to the anxiety scale, there were signs and symptoms of mild to moderate depression in patients with high need for insulin doses (the vast majority being reported by patients on a 4-dose per day regimen), hypocaloric and glycemic index increased above the upper limit of a diabetic patient.

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