Investigation of the effect of comorbid psychopathologies on glycemic control in children and adolescents with type 1 diabetes mellitus

Tip 1 diabetes mellituslu çocuk ve ergenlerde komorbid psikopatolojilerin glisemik kontrol üzerine etkisinin araştırılması

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SUMMARY

Objective: The presence of comorbid psychiatric conditions in chronic diseases makes the management of the disease difficult. Our study, we aimed to examine the relationship between psychiatric comorbid conditions and glycemic control in children and adolescents with Type 1 Diabetes. **Method:** In our study, depending on the number of patients, good and moderate controls were evaluated as a single group, and HbA1c levels of 8.5 and below were included in this group. Children for Depression Inventory (CDI), Screen for Child Anxiety-Related Emotional Disorders (SCARED), Turgay Child and Adolescent Behavioral Disorders Based on DSM-IV Screening and Evaluation Scale were applied. The case and parents were evaluated with K-SADS-PL.Among 778 diabetic patients who were followed up in the pediatric endocrinology clinic, 73 cases between the ages of 8 and 17 who were followed up regularly, who did not have any comorbidities and who accepted to participate in the study were evaluated psychiatrically. **Results:** Of the 73 cases included in the study, 29 were accepted as the patients with good glycemic control (HbA1c≤8.5 mg / dl), and 44 as with poor glycemic control (HbA1c> 8.5mg / dl). In cases with poor glycemic control, parents' education level and income level were significantly lower, while the rate of attention deficit and hyperactivity disorder, major depressive disorder, social anxiety disorder and psychopathology was significantly higher. **Discussion:** The findings of this study revealed that there are many factors affecting glycemic control and there is a strong relationship between glycemic control and psychopathologies.

Key Words: Type 1 diabetes mellitus, children, adolescents, adhd, psychiatric disorder

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ÖZET

Amaç: Kronik hastalıklarda eşlik eden psikiyatrik durumların varlığı, hastalığın yönetimini zorlaştırmaktadır. Çalışmamızda Tip 1 Diyabetli çocuk ve ergenlerde psikiyatrik eştanı durumları ile glisemik kontrol arasındaki ilişkiyi incelemeyi amaçladık. **Yöntem:** Çalışmamızda hasta sayısına bağlı olarak iyi ve orta kontroller tek grup olarak değerlendirildi, HbA1c düzeyi 8.5 ve altında olan olgular bu gruba dahil edildi. Çocuklar İçin Depresyon Ölçeği (ÇDÖ), Çocuklarda Anksiyete Tarama Ölçeği (ÇATÖ), Turgay Çocuk ve Ergen Davranış Bozuklukları DSM-IV'e Göre Tarama ve Değerlendirme Ölçeği uygulandı. Olgu ve ebeveynleri K-SADS-PL ile değerlendirildi. Çocuk endokrinoloji polikliniğinde takip edilen 778 diyabetik hastadan 8-17 yaşları arasında düzenli takipleri yapılan, ek hastalığı olmayan ve çalışmaya katılmayı kabul eden 73 olgu psikiyatrik olarak değerlendirildi. **Bulgular:** Çalışmaya alınan 73 olgunun 29'u glisemik kontrolü iyi (HbA1c≤8.5 mg/dl), 44'ü glisemik kontrolü kötü (HbA1c> 8.5mg/dl) olarak kabul edildi. Glisemik kontrolü zayıf olan olgularda anne-baba eğitim düzeyi ve gelir düzeyi anlamlı olarak daha düşük, dikkat eksikliği ve hiperaktivite bozukluğu, majör depresif bozukluk, sosyal anksiyete bozukluğu ve psikopatoloji oranları anlamlı olarak daha yüksekti. **Sonuç:** Bu çalışmanın bulguları, glisemik kontrolü etkileyen bir çok faktör olduğunu ve glisemik kontrol ve psikopatolojiler arasında güçlü bir ilişki olduğunu ortaya koymuştur.

Anahtar Sözcükler: Tip 1 diabetes mellitus, çocuklar, ergenler, DEHB, psikiyatrik bozukluk

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INTRODUCTION

Type 1 diabetes mellitus (DM) is an endocrinological disease associated with insufficient insulin secretion. Type 1 DM is one of the most frequently diagnosed chronic diseases in childhood. Its incidence and prevalence varies by country. The prevalence in a study published in 2017 were found to be 0.75 /1000 in Turkey (1). The annual incidence in our region has been determined as 7.2 / 10 thousand (2). Children and adolescents with type 1 DM are under risk in terms of psychiatric diseases due to the psychological burden brought by diabetes compared to the healthy population. Studies have found 2-3 times more psychiatric illnesses than the healthy population. It is known that depression, anxiety disorder, and attention deficit hyperactivity disorder (ADHD) are the most common psychiatric diagnoses (3).

Since cognitive and emotional abilities are not yet grown in children and adolescents, it is difficult to cope with diabetes on their own (4). When comorbid psychiatric diseases are added to the chronic disease manifestation, it becomes more difficult to manage diabetes. Short and long-term complications such as severe hypoglycemia attacks, hyperglycemia, obesity and microvascular disorders can be seen frequently in these cases. Patients with severe hypoglycemia attacks, obesity, or growth-developmental retardation may have internalizing symptoms (such as guilt, insecurity, avoidance of social environments, sadness, eating problems) due to social anxiety. This may lead to psychiatric disorders such as depressive disorder and anxiety disorder. In addition, it was found that disorders such as depressive and anxiety disorders were more common in patients with poor glycemic control and the presence of them has been found to be associated with glycemic control (4, 5).

Attention deficit and hyperactivity disorder is one of the most common neurodevelopmental disorders of childhood. This disease causes loss of function in academic and social areas in individuals (6). Among the basic symptoms of ADHD, there are symptoms related to the attention area such as inability to organize daily tasks and activities, forget fulness in daily activities, avoiding and delaying tasks, and inadequate organizational skills. (6). This situation makes it difficult to manage a chronic disease. Recent studies have shown that metabolic controls of type 1 DM cases diagnosed with ADHD are worse than those without ADHD (7, 8).There is no study in the literature examining good and bad glycemic control separately.

In this study, it was aimed to investigate the effect of comorbid psychopathologies on glycemic control in children and adolescents with type 1 DM. However, investigating the effect of other sociodemographic factors on glycemic control is another aim of the study.

METHOD

Participants

The cases participating in this study were selected from the cases with type 1 DM who were followed up in Gazi Yaşargil Training and Research Hospital Pediatric Endocrinology Unit. The inclusion criteria were determined as; the patient and her family agreed to participate in the study, had been diagnosed with Type 1 DM for at least one year and came for a check-up at least 4 times a year, the cases were between the ages of 8 and 17, the patient and the parent were literate, had no obstacle to filling the forms, the patient were using insulin injection method in the treatment. In the study, 778 patients with type 1 DM who were followed up in the pediatric endocrinology clinic were screened. Of the 79 cases who accepted to participate in the study and met the criteria, 5 were excluded from the study because they filled the forms incompletely and 1 case had mental retardation clinically. The study was completed with 73 cases.

The procedure

Approval was obtained from Diyarbakır Health Sciences University Gazi Yaşargil Training and Research Hospital Clinical Research Ethics Committee for the study (ethics committee decision dated 15.03.2020, numbered 474). After the study approval was obtained, the patients who

came to the Pediatric Endocrinology unit for control were referred to the child and adolescent psychiatry clinic. A brief preliminary interview was made to the cases meeting the criteria and evaluated. The patients and the parents (at least one parent or both) dealing with the patient during the clinical follow up of diabetes were assessed. Semi-structured psychiatric interviews and scales were used.

Measurements

Sociodemographic data form: The form which is prepared by the researchers contained sociodemographic data (age, gender, education level, socioeconomic level, parental age, education level, etc.) and clinical information about type 1 DM (HbA1c, annual number of hospitalizations, number of intensive care admissions, etc.).

Schedule for Affective Disorders and Schizophrenia for School-Age Children (Kiddie-SADS Lifetime Version) (K-SADS-PL): It is a semi-structured diagnostic interview developed to describe the past and present psychopathologies of children and adolescents according to DSM-4 diagnostic criteria (9). K-SADS-PL is administered through interviews with parents and the child, and is finally evaluated based on information from all sources. The final decision on diagnosis is based on the clinician's opinion. This interview is applied between the ages of 6-18. The Turkish version was adapted to DSM-5 (10).

Children for Depression Inventory-CDI: Adapted from Beck depression scale. The Turkish validity and reliability study of the form consisting of 27 questions was conducted. Each item evaluates the child's last two weeks. The answers given are scored between 0 and 2. The cut-off point of the form, which can be used between the ages of 6-17, was determined as 19. Maximum 54 points can be obtained from CDI, which is a self-report scale. The higher the scores obtained on the scale, the higher the severity of depression. (11,12)

Screen for Child Anxiety-Related Emotional Disorders (SCARED): It was developed by Birmaher et al. for screening childhood anxiety disorders. Turkish validity and reliability of the scale was made by Çakmakçı. It has parent and child forms. It is accepted that a score of 25 and above in SCARED, which consists of 41 items in total, is a warning for anxiety disorder. The scale also includes somatic-panic, generalized anxiety, separation anxiety, social anxiety, and school phobia subscales (13,14).

Turgay Screening and Evaluation Scale for Behavioral Disorders in Children and Adolescents Based on DSM IV: Screening and Evaluation Scale for Conduct Disorders in Children and Adolescents Based on DSM-IV was prepared by Atilla Turgay by considering DSM-IV diagnostic criteria. With this scale, ADHD, ODD (oppositional defiant disorder) and CD (behavioral disorder), which are disruptive behavioral disorders, are screened and evaluated. In this scale consisting of 41 questions in total, 9 questions are for attention deficit, 9 questions for hyperactivity, 8 questions for ODD and 15 questions for CD screening and evaluation. Each question may be answered as "no answer, a little, more and too much" (15, 16).

HbA1c (Glycosylated Hemoglobin): It is a marker that provides information about the glycemic index in the last 3 months, used in routine controls. It also predicts the risk of complications due to diabetes. Its normal range is stated to be 4.3-5.8%. For diabetic cases, below 7.5% are considered good control, 7.5-8.5% range as moderate control, and over 8.5% as poor glycemic control (17). In our study, depending on the number of patients, good and moderate controls were evaluated as a single group, and HbA1c levels of 8.5 and below were included in this group.

Statistical analysis

The data of the cases included in the study were recorded in the SPSS 22.0 program. In the normality test, it was determined that the data were suitable for normal distribution. In the study, independent sample t test was used for nominal data and chi-square test was used for categorical data. P value less than 0.05 was considered significant.

RESULTS

Of the 73 cases participating in the study, 29 were accepted as to have good glycemic control (HbA1c% ≤8.5 mg / dl), and 44 as with poor glycemic control (HbA1c%> 8.5mg / dl). The mean age of the cases was 13.5 (SD ± 2.4, min: 8.9 max: 17.8), 53.4% (n = 39) were female and 46.6% (n = 34) were male. Sociodemographic and clinical information of the cases are shown in Table 1.

While there was no psychiatric diagnosis according to K-SADS and scale scores in 37% of the cases (n = 27), at least one psychiatric diagnosis was found in 63% (n = 46). The most detected diagnosis proportionally in the cases is ADHD (28.7%). The distribution of psychiatric diagnoses of the cases by groups was shown in Table 2. ADHD, major depressive disorder (MDD) and social anxiety disorder (SAD) were significantly higher in patients with poor glycemic control.

Regardless of the glycemic status, those with and without psychopathology were evaluated in terms of age distribution. The mean age of those with psychopathology (n = 46) was 13.6 (SD ± 2.4), and the mean age of those without psychopathology (n = 27) was 13.3 (SD ± 2.41). No significant difference was found in terms of age distribution (independent sample t test p <0.05).

Table 1. The sociodemographic-clinical characteristics of the cases

	Good glycemic control (n=29)	Poor glycemic control (n=44)	P
Gender	Male: 48.3 % (n=14) Female:51.7 % (n=15)	Male: 43.2% (n=19) Female: 64.1 % (n=25)	0.474*
Age (year)	13.2 (SD 2.6)	13.7 (SD 2.3)	0.326**
HbA1c(%)	7.24 (SD 0.7)	10.8 (SD 1.5)	0.001*
Number of annual hospitalization	0.4 (SD 0.7)	1.9 (SD 1.2)	0.001*
Number of hospitalizationin ICU	0.4 (SD 0.6)	0.7 (SD 0.8)	0.037*
Maternal age (y l)	40.3 (SD 6.9)	40.7 (SD 6.8)	0.805**
Paternal age (y l)	44.3 (SD 7.2)	44.4 (SD 6.6)	0.942**
Maternal educational status	literate: 20.7% (n = 6) primary school graduate: 31% (n = 9) secondary school graduate: 6.9% (n = 2) high school graduate: 24.1% (n = 7) university graduate: 17.2% (n = 5)	literate: 50% (n = 22) primary school graduate: 36.4% (n = 16) secondary school graduate: 9.3% (n = 4) high school graduate: 2.3% (n = 1) university graduate: 2.3% (n = 1)	0.002*
Paternal educational status	literate: 0% (n = 0) primary school graduate: 27.6% (n = 8) secondary school graduate: 10.3% (n = 3) high school graduate: 20.7% (n = 6) university graduate: 41.4% (n = 12)	literate: 20.5% (n = 9) primary school graduate: 47.7% (n = 21) secondary school graduate: 6.8% (n = 3) high school graduate: 18.2% (n = 8) university graduate: 6.8% (n = 3)	0.001*
Income level (TL)	2300 TL and below: 27.6% (n = 8) 2300 TL and 5000 TL: 48.3% (n = 14) Over 5000 TL): 24.1% (n = 7)	2300 TL and below: 79.5% (n = 35) 2300 TL and 5000 TL: 18.2% (n = 8) Over 5000 TL: 2.3% (n = 1)	0.001*
School attendance	Yes: 96.6% (n = 28) None: 3.4% (n = 1)	Yes: 88.6% (n = 39) None: 11.4% (n = 5)	0.228*

Table explanation: SD: standard deviation, * chi-square test p <0.05, ** independent sample t test p <0.05

Table 2. Distribution of psychiatric diagnoses of the cases

		Good glycemic control	Poor glycemic control	Total	P
ADHD	Yes	10.3% (n=3)	40.9% (n=18)	21	0.007
	None	89.7% (n=26)	59.1% (n=26)	52	
ODD	Yes	3.4% (n=1)	9.1 % (n=4)	5	0.642
	None	96.6% (n=28)	90.9 % (n=40)	68	
adjustment disorder	Yes	6.9% (n=2)	13.6% (n=6)	8	0.465
	None	93.1 % (n=27)	86.4 % (n=38)	65	
MDD	Yes	0 % (n=0)	18.2 % (n=8)	8	0.019
	None	100% (n=29)	81.8 % (n=36)	65	
SAD	Yes	6.9% (n=2)	34.1% (n=15)	17	0.010
	None	93.1% (n=27)	65.9 % (n=29)	56	
OCD	Yes	3.4 % (n=1)	0 % (n=0)	1	0.397
	None	96.6% (n=28)	100% (n=44)	72	
GAD	Yes	3.4% (n=1)	11.4% (n=5)	6	0.392
	None	96.6% (n=28)	88.6% (n=39)	67	
STUTTERING	Yes	3.4% (n=1)	0% (n=0)	1	0.397
	None	96.6 % (n=28)	100% (n=44)	72	
ENURESIS	Yes	0 % (n=0)	4.5% (n=2)	2	0.514
	None	100% (n=29)	95.5% (n=42)	71	
Psychopathology	Yes	34.5% (n=10)	81.8% (n=36)	46	0.001
	None	65.5% (n=19)	18.2% (n=8)	27	

ADHD: Attention deficit and hyperactivity disorder, ODD: Oppositional defiant disorder, MDD: Major depressive disorder, SAD: Social anxiety disorder, OCD: Obsessive -compulsive disorder, GAD: Generalized Anxiety disorder
chi-square test p <0.05

DISCUSSION

In this study, cases with good and poor glycemic control followed with type 1 DM diagnosis were compared in terms of sociodemographic and clinical characteristics and comorbid psychiatric disorders. The two groups were determined according to their HbA1c levels. The annual number of hospitalizations and the number of intensive care hospitalizations of these two groups are also statistically significantly different. Groups that were statistically similar in terms of gender and age distribution were found to be significantly different in terms of maternal education level, father education level and income levels (p <0.005). As expected, in cases with poor glycemic control, maternal education level, father education level and income level were found to be significantly lower. These findings are consistent with previous studies. Parents have an

important role in the management of type 1 diabetes. In a study evaluating glycemic control and maternal education levels, a significant positive correlation was found between maternal education level and glycemic control. However, unlike our study, no significant relationship was found between income level and glycemic control in the same study (18). In a study comparing two different ethnic groups; a positive relationship was found between income level and glycemic index (19). In a study conducted in 2011, it was shown that most of the patients who reach the good glycemic index, which is their goals in diabetes treatment, have a high education level of their mothers (20). In a study examining the relationship between the education level of mothers and fathers, profession and metabolic control in Iran; it was found that high education level of both parents was positive for metabolic control. In addition, in this study, it was seen that the mother's having a job was also effective on metabolic control (21). In a study evaluating 259 children and their families in Jordan in 2019, low maternal education level and low income level were found to be associated with poor metabolic control (22). Studies emphasize that family factor is also important in type 1 DM, as well as medical and technical factors. In terms of school attendance, no significant difference was found between the two groups. In our study, both the subjects in the good glycemic control group (96.6%) and the patients in the poor glycemic control group (88.6%) were mostly attending school. No study comparing good glycemic control with poor glycemic control in terms of school dropout could not be found in the literature. However, in a study compared with healthy controls, it was found that the diabetic group had higher rates of absenteeism and school dropout (23). In a study conducted abroad, it was shown that it is associated with more absenteeism in patients with poor glycemic control (24).

In our study, the rate of psychiatric comorbidity was found to be statistically significantly higher in cases with poor glycemic control ($p < 0.05$). It is known that the frequency of psychiatric disorders in Type 1 DM cases is higher than the general population. In a long follow-up study conducted in Sweden, cases of type 1 diabetes and their healthy siblings were compared in terms of psychiatric comorbidity and suicide attempts. It has been shown that the frequency of psychiatric illness and suicide attempts is higher in cases followed up to the age of 18 after being diagnosed with type 1 diabetes (25). Various studies have shown that patients with type 1 diabetes have a higher rate of psychiatric comorbidity in patients with poor glycemic levels and high HbA1c levels (29, 20). Likewise, it is known that patients with psychiatric comorbidity also have poor metabolic outcomes. In other words, in children and adolescents with type 1 DM; there is a two-way relationship between comorbid psychopathologies and glycemic control. However, adolescence is known as the period in which psychiatric disorders are most common. In a study evaluating risk factors in terms of psychiatric disorders, the age range of 10-15 was given as the most risky age range (17). In our study, when the age distribution of those with and without psychopathology independent of glycemic status was examined, no significant difference was found between the two groups ($p > 0.05$). However, the age range in this study is similar to our study.

In our study, ADHD, MDD and SF were statistically significantly higher in patients with poor glycemic control than in patients with good glycemic control ($p < 0.05$). No significant difference was found for other psychopathologies. In a study conducted in our country, HbA1c levels were found to be associated with ADHD and MDD diagnoses. In this study in which 60 cases and their parents were evaluated, it was observed that ODD and conduct disorder diagnoses were also predictors for HbA1c (8). In our study, there was no patient with conduct disorder. There was no significant difference between the two groups for the diagnosis of ODD. Similar to the results of the study, it was found that ADHD and MDD diagnoses were higher in patients with poor glycemic levels. In a study conducted in our country with 75 patients with type 1 DM, the most common diagnosis was ADHD followed by MDD, anxiety disorder, and eating disorder (27). In a retrospective study with a large sample, 56722 pediatric diabetes cases were screened, and those with and without ADHD were compared. Poor glycemic control (high HbA1c, insulin level, body mass index, systolic blood pressure) was found in the diabetic patient group with ADHD (7). The most important reason for the poor prognosis of the glycemic index is poor

compliance with treatment (such as timely use of insulin, diet). These results support the hypothesis of our study, as attention problems, decision-making and organizational skills, and executive functions will be affected in ADHD and other psychiatric disorders. In a study comparing diabetic patients and healthy controls, 184 patients aged 6-14 years were evaluated. Anxiety and depression rates were found to be higher in diabetic patients than in the healthy group. In addition, poor treatment compliance and poor glycemic control were significantly higher in these cases (26). In a study in which 150 adolescents were evaluated, a positive relationship was found between high depression and anxiety levels and high HbA1c levels. However, anxiety disorders are not differentiated (28). Although there are many studies in the literature that examine the depression and anxiety levels of diabetic patients, there are a limited number of studies evaluating social anxiety and other anxiety disorders. In a study comparing adolescents with diabetes between the ages of 12-15 with healthy controls, social anxiety disorder was found to be significantly higher in the diabetic group (29). Similarly, in a study conducted in 2002, it was determined that social anxiety affects HbA1c levels (30). Patients who are afraid of hypoglycemia may reduce the insulin dose or postpone insulin injection or exhibit overnutrition due to social concerns. This may explain poor glycemic control in social phobic cases.

The limitations of the study were the small sample size and the recruitment of cases for six months. Studies with long follow-up and large samples are needed in this field.

CONCLUSION

As a result, there are many factors affecting glycemic control. The most important of these factors are the family factor and the psychiatric status of the case. In our study, we found that parental education level and income level were lower, whereas the rate of psychopathology (ADHD, MDD, SF) was significantly higher in cases with poor glycemic control. Therefore, in addition to routine metabolic monitoring of diabetes, psychiatric support and economic support opportunities for the family should be reviewed if psychiatric follow-up of the child and adolescent is necessary.

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