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RESEARCH

Anxiety and depression in adolescents with beta thalassaemia major

Beta talasemi majör tanılı ergenlerde anksiyete ve depresyon

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Abstract

Purpose: The course of Beta Thalassaemia Major triggers children's susceptibility to anxiety and depressive mood. The aim of this study was to determine the frequency of anxiety and depression in adolescents with Beta Thalassaemia Major and its relationship with hospitalisation.
Materials and Methods: This correlational case-control study was conducted with a total of 77 healthy children (case=39, control=38) with a confirmed diagnosis of major thalassaemia. The data were collected using the "Descriptive Information Form", Revised Child Anxiety and Depression Scale - Child Version (RCADS-CV) and Hospital Anxiety and Depression (HAD) Scale.
Results: When the comparison of the mean RCADS-CV scores according to the groups was analysed, it was found that the mean Major Depressive Disorder sub-dimension score was significantly higher in the case group. It was found that 61.5% of the children in the case group and 92.1% of the children in the control group experienced moderate depression and the difference was statistically significant. In addition, when the RCADS-CV cut-off score of 71 and above was evaluated, it was found that 12.8% of children with Beta Thalassaemia Major had a pathological picture.
Conclusion: The high prevalence of major depressive disorders in children with Beta Thalassaemia Major and hospitalisation-related depression levels in healthy children is highly significant.
Keywords:. Thalassaemia, anxiety, depression, nursing care, adolescents.

Öz

Amaç: Beta Talasemi Majör seyri çocuklarda anksiyete ve depresif ruh haline yatkınlığı tetikler. Bu çalışmanın amacı Beta Talasemi Majörlü ergenlerde anksiyete ve depresyon sıklığını ve bunun hastaneye yatışla ilişkisini belirlemektir.
Gereç ve Yöntem: Bu korelasyonel vaka-kontrol çalışması, majör talasemi tanısı doğrulanmış toplam 77 sağlıklı çocukla (vaka=39, kontrol=38) yürütülmüştür. Veriler "Tanımlayıcı Bilgi Formu", Revize Çocuk Anksiyete ve Depresyon Ölçeği - Çocuk Versiyonu (RCADS-CV) ve Hastane Anksiyete ve Depresyon (HAD) Ölçeği kullanılarak toplandı.
Bulgular: Gruplara göre ortalama RCADS-CV puanlarının karşılaştırılması incelendiğinde, Majör Depresif Bozukluk alt boyut puanının ortalama vaka grubunda anlamlı derecede yüksek olduğu bulunmuştur. Vaka grubundaki çocukların %61,5'inin, kontrol grubundaki çocukların ise %92,1'inin orta düzeyde depresyon yaşadığı ve aradaki farkın istatistiksel olarak anlamlı olduğu bulunmuştur. Ayrıca, RCADS-CV kesme puanı 71 ve üzeri olarak değerlendirildiğinde, Beta Talasemi Majörlü çocukların %12,8'inin patolojik bir tabloya sahip olduğu bulunmuştur.
Sonuç: Beta Talasemi Majörlü çocuklarda majör depresif bozuklukların yüksek prevalansı ve sağlıklı çocuklarda hastaneye yatışla ilişkili depresyon düzeylerinin yüksek olması oldukça anlamlıdır.

Anahtar kelimeler: Talasemi, anksiyete, depresyon, hemşirelik bakımı, ergenler.

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INTRODUCTION

A chronic disease is a condition that requires lifelong support, protection, intermittent monitoring, and continuous treatment[1]. Childhood chronic diseases are gradually increasing and are an important health problem in many countries worldwide. Epidemiological studies in the literature indicate that one out of every four children has a chronic disease[2].

Thalassaemia is a common form of inherited anemia. One of the most common inherited single-gene diseases is β-thalassaemia[3]. It is an important public health problem in Mediterranean countries, including Turkey. In 1971, Cavdar and Arcasoy[4] reported that the overall incidence of b-thalassemia was 2.1%. There are about 1.5 million thalassemia patients and about 5500 patients with thalassemia and hemoglobinopathies in Turkey[4,5].

Like all chronic patients, Beta Thalassaemia Major (BTM) patients are vulnerable to emotional and behavioral problems[6]. The majority of children with thalassemia are reported to have psychological problems such as anxiety and depression due to regular hospital visits for blood transfusions and frequent absences from school[7–9]. Understanding the relationship between chronic diseases and depressive disorders is extremely important in terms of public health assessment, as depressive disorders follow a chronic course when left untreated[10].

Although great advances have been made in treating BTM in recent years and complication rates have decreased, studies show that even in developed countries, patients' quality of life is still lower than in the general population[3,6,8]. Various measures of patient exposure, comorbidities, and psychological disorders such as depression, anxiety, transfusions, time spent on treatment, and follow-up of complications hurt daily life[6,9,11].

In addition, the course of the disease causes children's social activities to be restricted, physical and facial deformities, fear of separation from the family or death, and triggers their susceptibility to anxiety and depressive moods[11,12]. However, another dimension of the studies emphasizes that children with chronic diseases have depression and anxiety scores comparable to physically healthy children. These studies emphasize that the type of chronic disease, high self-esteem, and maternal/family support are essential protective factors[13].

Although hospital inpatient treatment in children is mainly used for acute health problems, hospitalization of children with chronic illness can be severe enough to affect growth, development, self-esteem, school success, or social relationships[14]. Studies have found that BTM, which is one of the chronic diseases, leads to negative body perception and low self-esteem[6,15,16]. This low self-esteem is expected to increase the prevalence of anxiety and depression and adversely affect children's future lives. Many studies[6,9,11,12,16,17] have evaluated psychiatric disorders in thalassemia patients, but relatively little is known about the predictors of these disorders. Therefore, this study aimed to evaluate the prevalence of anxiety and depression in Turkish children with BTM to determine their relationship with hospitalization and their predictors.

MATERIALS AND METHODS

Sample

Patients admitted to the Pediatric Haematology Oncology Clinic and Healthy Child Outpatient Clinic of a hospital in Adana, Türkiye between February 2022 and February 2023 were included in the study. The study population consisted of all children between the ages of 10-18 diagnosed with BTM who were treated as outpatients or inpatients at the hospital in the said date range. The study population consisted of 172 children who received inpatient or outpatient treatment services in the hospital on the date of the study. The criteria for inclusion in the case group were as follows.

1. To be between the ages of 10-18,
2. To have been diagnosed with Beta Thalassaemia Major for at least 6 months,
3. To have adequate Turkish receptive-expressive language skills,
4. To agree to participate in the study,
5. To have no visual or hearing problems,
6. To have been given written consent by the family to participate in the study,
7. Not to have received a psychiatric diagnosis (anxiety disorder, depression, etc.) for the last month and not to be receiving treatment for this reason.

Inclusion criteria for the control group:

1. To be between the ages of 10-18
2. Sufficient level of receptive-expressive language skills in Turkish,
3. To agree to participate in the study

4. Not have vision and hearing problems.
5. Not to be diagnosed with a chronic disease and not receive treatment.
6. Not having a psychiatric diagnosis (anxiety disorder, depression, etc.) for the last month and not being treated for this reason.

The study sample consisted of 77 children (case: 39, control: 38) who met the inclusion criteria and volunteered to participate. On the other hand, participants who were under the age of 10 (n=40), who had insufficient Turkish reading comprehension skills due to being refugees in the province where the study was conducted (n=80), who were newly diagnosed (n=24), and who had not completed the questionnaire (n=13) were excluded from the study.

Procedure

The study was approved by the Clinical Studies Ethics Committee of Adana City Training and Education Hospital in Adana (Date: 10.02.2022, Decision No: 1767), and institutional permission was obtained. The study's rationale and the purpose for which the results would be used were explained to the adolescents participating in the study and their families, and their consent was obtained. The study adhered to the ethical principles outlined in the Declaration of Helsinki.

All patients were examined by the investigating Paediatric Haematology and Oncology Specialist (DAT) for the presence of Mongoloid facial appearance with tanned skin, short stature, delayed puberty, diabetes, heart failure, and liver failure.

Measures

The researchers used the "Introductory Information Form, "Revised Child Anxiety and Depression Scale—Child Version," and "Hospital Anxiety and Depression Scale," which included the children's sociodemographic and clinical characteristics.

Questionnaire form

The researchers developed this form to evaluate the sociodemographic and clinical characteristics of the participants. It is a questionnaire consisting of 30 questions, including sociodemographic characteristics such as age, gender, height, weight, educational status, and income level, as well as clinical characteristics such as transfusion frequency, type of iron chelation, presence of splenectomy, results of some blood values, and history of psychiatric disorder.

Revised Child Anxiety and Depression Scale – Child Version (RCADS-CV)

RCADS [18] is a 47-item instrument developed by Chorpita et al. to measure DSM-IV-based symptoms of anxiety disorders and depression in children and adolescents. Gormez et al. [19] performed Turkish validation of the scale. In a clinical sample, the RCADS-CV provides an overview of the severity of depression and the depressive symptom profile. The scale can provide information not only in the diagnosis but also in the measurement of the response to treatment at the beginning and during the follow-up period following the diagnosis of the disease. The scale consists of a total of six sub-dimensions. These subscales correspond to seven items for Separation Anxiety Disorder (SAD), nine items for Social Phobia (SP), six items for Obsessive Compulsive Disorder (OCD), nine items for Panic Disorder (PD), six items for Generalised Anxiety Disorder (GAD) and ten items for Major Depressive Disorder (MDD). It is scored on a 4-point scale (0 = never, 1 = sometimes, 2 = often and 3 = always). The scores are converted into T-scores, allowing the distance from the mean for age and gender to be calculated (1.5 standard deviations). While there was a positive correlation between the high T score and the depressive mood of the child, a T score above 70 was considered pathological. The internal consistency of the subscales of the RCADS-CV is high, with Cronbach's alpha values ranging from 0.78 to 0.88. Cronbach'sCronbach's alpha value for this study is 0.96.

Hospital Anxiety and Depression Scale (HADS)

Hospital Anxiety and Depression Scale was developed by Zigmond and Snaith [20]. Turkish validity and reliability for adolescent age groups was conducted by [21]. The HADS is a self-assessment scale used for screening, not diagnostic purposes. The fourteen-item HADS includes a mixed 7-item HADS Anxiety subscale and HADS Depression subscale. In each item, a score between 0-3 is obtained by choosing four options. The items are marked according to how the respondent has felt in the last week.

Items 1, 3, 5, 6, 8, 10, 11 and 13 show decreasing severity and are scored as 3, 2, 1, 0; items 2, 4, 7, 9, 12 and 14 are scored as 0, 1, 2, 3. For the anxiety subscale, the scores of items 1, 3, 5, 7, 9, 11, and 13

are summed; for the depression subscale, the scores of items 2, 4, 6, 8, 10, 12, and 14 are summed. By summing the subscale scores, 0-21 points can be obtained from each of the Depression and Anxiety subscales. For each subscale, it is stated that a score of 0-7 is a normal range, a score of 8-10 suggests the presence of a mood disorder, and a score of 11 and above indicates a possible mood disorder. Cronbach's α value of the scale is 0.818 for HADS Anxiety and 0.793 for HADS Depression. For this study, HADS Anxiety was 0.78, and HADS Depression was 0.63.

Height-Weight measurements

Height and weight measurements were performed using a KERN MPE 250K100PM stadiometer. The device was installed and calibrated before use. Weight measurement was taken with a digital scale sensitive to 100 grams. Care was taken to ensure that the individual wore as little clothing and no shoes as possible. During the measurement, individuals were ensured they did not receive support from anywhere and stepped on the scale evenly. BMI was calculated by the Weight (kg) / Height^2(m) formula. According to BMI values, 18.5–24.9 was average weight, 25.0–29.9 was pre-obesity, 30.0– 39.9 was obese, and above 40 was considered morbid obese [22].

Biochemical analysis

Within the scope of the study, various biochemical markers that may affect the anxiety and depression levels of the participants were studied. Laboratory indices included routine blood count and liver and kidney function. Blood samples were obtained by the same nurse working in the clinic from the children in the case group for some biochemical markers (white blood cell (WBC), platelet count, hemoglobin concentration, neutrophil and lymphocyte count, blood urea nitrogen (BUN), creatine, platelets, aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin, direct bilirubin, lactate dehydrogenase (LDH), direkt coombs etc). In the hematological examination, 5 mL of blood was taken from the vein to analyze various markers. In the study, analyses were based on hospital reference values, and the Dianagel Grifols brand device was used to determine blood groups. Beckman Coulter brand DxH 800 Haematology Analyzer was used for haemogram analysis, and AU5800 Clinical Chemistry and UniCel DxI 800 immunoassay systems were used for biochemistry analysis

Statistical analysis

The data obtained in the study were analyzed using SPSS (Statistical Package for Social Sciences) for Windows 25.0 software. Descriptive statistical methods (number, percentage, min, max, mean, standard deviation) were used to evaluate the data. The normal distribution of the data was analyzed using kurtosis and skewness values. An independent t-test for the difference between two independent groups was used to compare quantitative and normally distributed data. Mann Whitney U test was used to compare the two independent groups in terms of quantitative data and non-normally distributed data. In the analysis of categorical data, Pearson's chi-square test was used. An independent sample t-test and Mann-Whitney U-tests were used to analyze some laboratory results and compare HADS and RCADS-CV scores. Pearson Chi-Square test was used to analyze demographic data and some Clinical Characteristics [23].

RESULTS

The distribution of information about the demographic characteristics of the participants is provided in Table 1. It was observed that 61.5% of the participants in the case group were male, 38.5% were female, and 53.8% were under 13 years of age, 59% had a BMI below 18.50, and 84.6% lived in a nuclear family. In the control group, 42.1% of the participants were male, 57.9% were female, and 50% were under 13 years of age, 23.7% had a BMI below 18.50, and 100% lived in a nuclear family. When the results were analyzed, it was determined that the case and control groups showed homogeneous distribution according to the gender, age, and place of residence of the participants ($p>0.05$). It was determined that the weights, height, and BMI values of the participants in the case and control groups showed a statistically significant difference in the case and control groups ($p<0.05$). The case group's weights, height, and BMI values were lower than those of the control group.

When the relationships of some clinical characteristics of the participants between the case and control groups were analyzed, it was seen that 41% of the participants in the case group and 7.9% of the participants in the control group experienced fatigue, and the difference was statistically significant ($p<0.05$). It was observed that 30.8% of the participants in the case group and 7.9% of the

participants in the control group experienced anorexia, and the difference was statistically significant ($p<0.05$). It was observed that 61.5% of the participants in the case group and 2.6% in the control group had an abnormal facial appearance, and the difference was statistically significant ($p<0.05$). It was determined that 30.8% of the participants in the case group experienced enlargement and thinning of the bones, 17.9% experienced restlessness, and 61.5% experienced pallor, while the participants in the control group did not experience this condition ($p<0.05$).

Table 1. Distribution of demographic characteristics of the participants

		Group				*Total*		*Chi square*	*p value*
		Case		**Control**					
		Number	**Percentage**	**Number**	**Percentage**	**Number**	**Percentage**		
Gender	Female	15	38,5	22	57.9	37	48.1	2.912 P	0.088
	Male	24	61.5	16	42.1	40	51.9		
Age (year)	<= 13.00	21	53.8	19	50.0	40	51.9	0.766P	0.682
	14.00 – 15.00	9	23.1	12	31.6	21	27.3		
	16.00+	9	23.1	7	18.4	16	20.8		
BMI	<18.5	23	59.0	9	23.7	32	41.6	**12.551FE**	**0.002***
	18.5-24.9	15	38.5	21	55.3	36	46.8		
	25.0-29.9	1	2.6	8	21.1	9	11.7		
Family type	Nuclear	33	84.6	38	100.0	71	92.2	**4.380YC**	**0.036***
	Extended	6	15.4	0	0.0	6	7.8		
Place of settlement	Adana	37	94.9	38	100.0	75	97.4	0.487YC	0.485
	Outside Adana	2	5.1	0	0.0	2	2.6		
Educational status	Primary School	12	30.8	2	5.3	14	18.2	**17.676 P**	**0.000***
	Middle school	21	53.8	14	36.8	35	45.5		
	High school	6	15.4	22	57.9	28	36.4		
Income level	Poor	17	43.6	2	5.3	19	24.7	**58.762 P**	**0.000***
	Medium	19	48.7	0	0.0	19	24.7		
	Good	3	7.7	36	94.7	39	50.6		
		Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	**t test**	**p value**
Age		13.64	1.99	13.87	1.82	13.75	1.90	-0.523	0.603
Body weight		36.08	8.46	51.12	12.75	43.50	13.12	**-6.083**	**0.000***
Length		139.67	10.56	155.75	11.09	147.60	13.46	**-6.516**	**0.000***
BMI		18.39	3.53	20.82	3.57	19.59	3.73	**-3.002**	**0.004***

*p<0.05 P: Pearson chi-square test; YC: Yates correction; FE=Fisher Exact Chi-square t: Independent sample t test BMI: Body Mass Index.

It was observed that 35.9% of the participants in the case group had hepatomegaly, 33.3% had splenomegaly, and 20.5% had splenectomy. In comparison, 2.6% of the participants in the control group had the related problem, and the difference was statistically significant ($p<0.05$). There was no statistically significant correlation between abdominal pain, muscle joint pain, and body pain in the case and control groups ($p>0.05$). The mean frequency of hospital visits was 8.13±5.32; the mean frequency of transfusion was 12.33±1.15; the mean age at chelation initiation (years) was 3.54±1.07; and the mean age at transfusion initiation (years) was 3.10±1.21 in the case group (Table 2).

Table 2. Comparison of some clinical characteristics of participants according to groups

		Case		Control		Total		Test value	p value
		n	%	n	%	n	%		
Fatigue	Yes	16	41.0	3	7.9	19	24.7	**11.366 P**	**0.000***
	No	23	59.0	35	92.1	58	75.3		
Abdominal pain	Yes	5	12.8	0	0.0	5	6.5	3.313 YC	0.069
	No	34	87.2	38	100.0	72	93.5		
Decreased appetite	Yes	12	30.8	3	7.9	15	19.5	**6.420 P**	**0.011**
	No	27	69.2	35	92.1	62	80.5		
Abnormal facial appearance	Yes	24	61.5	1	2.6	25	32.5	**30.460 P**	**0.000***
	No	15	38.5	37	97.4	52	67.5		
Bone enlargement and thinning	Yes	12	30.8	0	0.0	12	15.6	**13.851 P**	**0.000***
	No	27	69.2	38	100.0	65	84.4		
Muscle and joint pain	Yes	5	12.8	3	7.9	8	10.4	0.112 YC	0.738
	No	34	87.2	35	92.1	69	89.6		
Pallor	Yes	24	61.5	0	0.0	24	31.2	**33.974 P**	**0.000***
	No	15	38.5	38	100.0	53	68.8		
Discomfort	Yes	7	17.9	0	0.0	7	9.1	**5.488 YC**	**0.019***
	No	32	82.1	38	100.0	70	90.9		
Splenectomy	Yes	8	20.5	1	2.6	9	11.7	**4.355 YC**	**0.037***
	No	31	79.5	37	97.4	68	88.3		
Hepatomegaly	Yes	14	35.9	1	2.6	15	19.5	**13.579 P**	**0.000***
	No	25	64.1	37	97.4	62	80.5		
Splenomegaly	Yes	13	33.3	1	2.6	14	18.2	**12.195 P**	**0.000***
	No	26	66.7	37	97.4	63	81.8		
Body pain	Yes	3	7.7	1	2.6	4	5.2	0.237 YC	0.626
	No	36	92.3	37	97.4	73	94.8		
		Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	**t test**	**p value**
Transfusion start age		3.10	1.21	--	--	3.10	1.21		
Chelation start age		3.54	1.07	--	--	3.54	1.07		
Transfusion frequency year		12.33	1.15	--	--	12.33	1.15		
Hospital visit frequency		8.13	5.32	--	--	8.13	5.32		

P: Pearson chi-square test; YC: Yates correction; *$p<0.05$

When the comparison of some laboratory results of the participants in the case and control groups was analyzed, it was found that there was no statistically significant difference between the WBC, Platelet, Neutrophil, and Lymphocyte Count, BUN values of the participants ($p>0.05$). There was a statistically significant difference between the participants' hemoglobin, AST, ALT, total bilirubin, direct bilirubin, LDH, and creatinine values in the case and control groups ($p<0.05$). Accordingly, AST, ALT, total bilirubin, direct bilirubin, and LDH values of the case group participants were higher than those of the control group, while hemoglobin and creatinine values were lower (Table 3).

Table 3. Comparison of some laboratory results between case and control groups

	Case	**Control**		
Parameter (reference range)	**Mean±SD (Median) (Q1-Q3)**	**Mean±SD (Median) (Q1-Q3)**	**Test value**	**p value**
WBC (5980-13510 mcL)	6893.87±3473.7 (6600) (4300-8700)	6681.58±2247.02 (6650) (5000-7900)	-0.117[z]	0.907
Hemoglobin (10.1-12.5 g/dL)	9.16±1.15 (9.2) (8.5-9.9)	13±1.04 (12.9) (12.4-13.8)	**7.289[z]**	**0.000***
Platelet (206000-445000 mcL)	404889.74±262683.99 (308000) (239000-546000)	299000±135216.14 (272000) (227000-335000)	-1.447[z]	0.148
Number of Neutrophil (1091-7021 mcL)	4851.03±2775.78 (4300) (2900-5900)	4078.95±1092.52 (4100) (3300-4800)	-0.724[z]	0.469
Number of Lymphocyte (1560-7830 mcL)	2656.41±1713.84 (2000) (1700-3000)	2897.37±3369.38 (2000) (1600-3200)	-0.112[z]	0.911
AST (5-50 U/L)	42.64±26.26 (40) (28-47)	23.95±7.98 (22.5) (17-31)	**-4.937[z]**	**0.000***
ALT (5-50 U/L)	42.72±40.77 (36) (18-48)	17.08±7.82 (16) (11-20)	**-4.417[z]**	**0.000***
Total Bilirubin (0.3-1.2 mg/dL)	3.26±7.53 (1.8) (1.23-2.48)	0.55±0.3 (0.53) (0.36-0.57)	**-6.655[z]**	**0.000***
Direct Bilirubin (0-0.2 mg/dL)	0.41±0.16 (0.4) (0.29-0.53)	0.19±0.16 (0.11) (0.08-0.31)	**-5.176[z]**	**0.000***
LDH (180-430 U/L)	245.03±59.02 (240) (198-281)	213.97±88.74 (196) (178-232)	**-3.175[z]**	**0.002***
BUN (17-43 mg/dL)	25.79±7.8 (25) (20-32)	23.45±6.68 (22.35) (18-31)	-1.413[t]	0.162
Creatinine (0.15-0.37 mg/dL)	0.34±0.11 (0.32) (0.27-0.38)	0.42±0.11 (0.4) (0.34-0.5)	**-3.178[t]**	**0.002***

t: Independent sample t test; z: Mann Whitney U z value; *p<0.05
WBC: White Blood Cell; AST: Alanine Aminotransferase; AST: Aspartate Aminotransferase; BUN: Blood Urea Nitrogen; LDH: Lactate Dehydrogenase.

When the comparison of HADS and RCADS-CV scores according to the groups was analyzed, it was found that Hospital Depression scores, one of the sub-dimensions of the HADS, showed a statistically significant difference between the case and control groups ($p<0.05$). Depression scores of the control group were found to be higher than the case group. Hospital Anxiety scores did not show a statistically significant difference between the case and control groups ($p>0.05$). When the comparison of RCADS-

CV mean scores according to the groups was analyzed, it was found that MDD sub-dimension scores showed a statistically significant difference between the case and control groups ($p<0.05$). Depression scores of the control group were found to be lower than the case group. It was determined that there was no statistically significant difference between the other sub-dimensions and the total score of the scale ($p>0.05$) (Table 4).

Table 4. Comparison of HADS and RCADS-CV scores according to groups

	Group	**Mean±SD**	**t test**	p value
HADS Anxiety	Case	13.72±4.94	-1.776	0.080
	Control	15.58±4.22		
HADS Depression	Case	11.67±3.39	**-5.476**	0.000*
	Control	16.11±3.72		
RCADS-CV -SAD	Case	51.02±10.29	0.908	0.367
	Control	48.95±9.71		
RCADS-CV -SP	Case	49.95±10.46	-0.044	0.965
	Control	50.05±9.65		
RCADS-CV- OCD	Case	51.78±11.17	1.597	0.114
	Control	48.17±8.4		
RCADS-CV- PD	Case	50.24±11.25	0.214	0.831
	Control	49.75±8.68		
RCADS-CV- GAD	Case	51.35±12.38	1.215	0.229
	Control	48.61±6.64		
RCADS-CV- MDD	Case	52.54±11.47	**2.336**	0.023*
	Control	47.39±7.51		
RCADS-CV	Case	50.8±11.03	0.706	0.482
	Control	49.18±8.89		

*p<0.05 t: independent sample, t test SAD: Separation Anxiety Disorder, SP: Social Phobia, OCD: Obsessive Compulsive Disorder, PD: Panic Disorder, GAD: Generalised Anxiety Disorder, MDD: Major Depressive Disorder, RCADS-CV: Revised Child Anxiety and Depression Scale – Child Version, HADS: Hospital Anxiety and Depression Scale

There is no statistically significant correlation between anxiety HADS Anxiety and the groups ($p>0.05$). There is a statistically significant relationship between HADS Depression and groups ($p<0.05$). While 61.5% of the children in the case group had depression scores of 11 points and above, 92.1% of the children in the control group had depression scores of 11 points and above. While 28.2% of the children in the case group had depression scores between 8-10 points, 5.3% of the children in the control group had depression scores between 8-10 points. No statistically significant relationship was found between the groups according to the RCADS-CV cut-off score (Table 5) ($p>0.05$).

Table 5. Comparison of HADS and RCADS-CV levels according to groups

		Group				χ^2	p value
		Case		Control			
		Number	Percentage	Number	Percentage		
HADS Anxiety	Normal (0-7)	4	10.3	1	2.6	5.605	0.062
	Mild (8- 10)	9	23.1	3	7.9		
	Moderate (11,00+)	26	66.7	34	89.5		
HADS Depression	Normal (0-7)	4	10.3	1	2.6	**9.961**	**0.004***
	Mild (8- 10)	11	28.2	2	5.3		
	Moderate (11,00+)	24	61.5	35	92.1		
RCADS-CV	<= 70.00	34	87.2	38	100.0	3.313	0.069
	70.01+	5	12.8	0	0.0		

χ^2: Chi square test; *p<0.05, RCADS-CV: Revised Child Anxiety and Depression Scale – Child Version, HADS: Hospital Anxiety and Depression Scale

DISCUSSION

Changes and parameters that may affect quality of life and mental health in patients with chronic diseases are frequently encountered in the literature. The results of this study, which was conducted to examine the clinical features and to evaluate the relationship between hospital anxiety and depression in patients with BTM in adolescents in Turkey, are remarkable and have potential implications for future studies.

During adolescence, negative situations related to body image, identity, interpersonal relationships, and performance may cause anxiety. Adolescents are at risk for developing psychiatric disorders because they are more sensitive to their changing bodies[24,25]. During adolescence, when the socialization process is intense, adolescents who face obstacles caused by adverse health conditions may not be able to develop the necessary skills for adult life. This situation may cause the adolescent to be inadequate in coping with problems and not to develop self-confidence, anxiety, and depression[24]. In this study, in which we examined the difference in some sociodemographic and clinical characteristics in patients with and without BTM, it is seen that the gender and age distributions of the participants were homogeneous. The fact that similar results were obtained in both groups is one of the study's strengths. When Tables 1 and 2 are analyzed, it is seen that participants' BMI, family type, education level, and income level were more negatively affected in the case group compared to the control group. In addition, it is observed that some symptoms related to BTM (fatigue, loss of appetite, abnormal facial appearance, etc.) are more intense in the case group compared to the control group. This study shows that low educational level is the most significant sociodemographic difference between children with and without BTM. This can be explained by the negative impact of chronic anemia and its complications on the child's ability to learn, as well as the frequent absence from school for regular blood transfusions or the weakness/weakness associated with the disease [26]. However, an overprotective parenting style is more common among parents with sick children in Turkey; this style may prevent the child from going to school when he/she can go[27]. This finding is compatible with the results reported by other investigators in thalassemia patients[28,29]. A study conducted in India reported that 90% of students with thalassemia took several days off from school, affecting more than 70% of their academic achievement[30]. In the USA, Saraviet al.[31] reported that patients with thalassemia are exposed to many severe stressors, including frequent blood sampling for laboratory tests, multiple transfusions, and frequent administration of iron chelator drugs, which play an essential role in the development of anxiety. The results of this study suggest that painful interventions such as frequent hospitalization, interventional interventions, chelator agent use, and splenectomy may significantly affect school attendance and education levels.

Another study dimension examined the results of two scales, including mental health indicators and the differences between the groups (Tables 4 and 5). When the results were analysed, it was found that the Depression sub-dimension of the HADS scale was significantly higher in the control group, and the Major Depressive Disorder sub-dimension of the RCADS-CV scale was found to be higher in children with BTM. However, 61.5% of the children in the case group and 92.1% of the children in the control group experienced moderate depression related to hospitalization. Although there was no significant difference between the groups regarding the RCADS-CV scale, 12.8% of children with BTM had a pathological picture when the cut-off score was 71 and above. When the literature is examined, it is observed that anxiety levels vary between 20.5% and 58.4% in studies conducted with different scales[11,32,33]. The lower rates observed in our study may be related to the fact that the diagnosis of Major Depressive Disorder in our scale appears to be a more severe picture and that there is an increase in the quality of life of these children with the developing technology. In addition, no other study has been found to evaluate anxiety and depressive disorders in patients with BTM with the scale we used in our study.

Physical illnesses can have a negative psychiatric impact on children. These negativities may reduce adolescents' quality of life, slow their recovery, and even worsen it. In individuals hospitalized for any reason, thoughts about the disease or hospital environment may cause negative emotions and behaviors [34,35]. The children in the control group included in the study were healthy children without any chronic disease. Children with BTM regularly visit the hospital and know the hospital environment. Studies have emphasized that the most critical parameters affecting hospital fear are uncertainty, fear related to IV interventions, and relationships with healthcare professionals[34,36–38].

As a result of our study, the fact that the children in the control group had higher CFS depression scores compared to the case group may be related to the fact that the children in the case group had decreased hospital anxiety due to long-term hospital visits. In contrast, the children in the control group had high anxiety about the unknown. There is a need for long-term studies with more participants and including interventions that can reduce hospital depression.

Major depressive disorder (MDD) is characterized by a depressed mood or feeling of sadness and decreased interest in daily activities[39]. MDD can have significant effects when it occurs during childhood and adolescence. When the literature is examined, deterioration in school performance, difficulties in interpersonal relationships in adulthood, adolescent parenthood, other mental health disorders, and increased risk of substance use disorders have been associated with the diagnosis of MDD in childhood[40]. In 2016, an estimated 12.8% of the US population aged 12-17 years was diagnosed with at least one major depressive episode 41. In addition, 8% of adolescents diagnosed with MDD committed suicide in young adulthood, and it is the second leading cause of death among adolescents aged 12-17 years[42,43]. In our study, the increase in the MDD sub-dimension scores compared to the control group is significant. MDD is under-recognized and under-treated, as the presentation of MDD symptoms may differ from adults. Longitudinal studies with a larger population are needed in children with BTM.

There are some limitations in this study. Firstly, the data obtained are limited to adolescent groups. Since the study group is a specific age group, the number of participants is small. They cannot be generalized to all age periods. In addition, the data were evaluated in line with the personal answers given to the questions in the measurement tool.

When the thalassemia process is examined, it is seen that patients with thalassemia adapt to living with a chronic disease. However, the psychosocial problems and treatment burden they experience are considerable. Therefore, treatment and care for psychosocial problems should be emphasized. The psychosocial care model should be included in patient follow-ups. In addition, the cooperation of patients, families, and healthcare professionals is of great importance in improving the well-being and positive coping mechanisms of individuals with thalassemia.

Thalassemia major is closely associated with psychological conditions such as changes in body image and self-esteem due to bone deformities and growth retardation, and this relationship is clinically important. In chronic diseases, physical deficiencies and deformities may reduce self-esteem by distorting body image and creating a sense of inadequacy. In future studies, there is a need for long-term studies addressing the physical conditions of patients, self-

esteem, anxiety, and depression levels, especially in adolescence.

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Ethical Approval: The study was approved by the Clinical Studies Ethics Committee of Health Science University Adana Training and Education Hospital in Türkiye (Date: 10.02.2022, Decision No: 1767) and institutional permission was obtained. The rationale of the study and the purpose for which the results would be used were explained to the adolescents participating in the study and their families, and their consent was obtained. The study adhered to the ethical principles outlined in the Declaration of Helsinki.
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