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Evaluation of Psychosocial Morbidity among Children and Adolescents with Beta-Thalassemia Major

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ABSTRACT

Background: Thalassemia major (TM) is a long-term illness that affects the child and family emotionally and psychologically.

Aim: To assess the existence of psychiatric symptoms in thalassemia-affected children and teenagers, such as hysteria, somatic symptoms, obsessive symptoms, depressive symptoms, anxiety, and phobic anxiety.

Subjects and methods: This is a case-control study that included 42 children and adolescents who have transfusion-dependent beta-thalassemia major and 42 healthy controls. All patients underwent Psychological assessment using a questionnaire by The Arabic version of the Child Behavior Check List (CBCL/6-18).

Results: There was a significant difference between the two groups regarding total problems grades that were clinical and borderline in cases more than in the control group.

Conclusion: The Arabic version of the Child Behavior Check List identifies behavioral and psychological issues in patients with beta-thalassemia major.

Keywords: psychosocial, thalassemia major, children, adolescents.

INTRODUCTION

β-Thalassemia major is the most common hemoglobinopathy with a carrier rate of 9-10.2%, it is prevalent in the Mediterranean region, particularly in Egypt [(1)].

Because of the high costs of treatment, Beta thalassemia major is a significant health issue for the public health system of any nation, necessitating frequent hospitalizations, iron chelation, and general medical follow-up. This places a strain on the healthcare system as well as the affected families' children, who are made more susceptible to behavioral, emotional, social, and psychological problems[(2)].

Depending on the severity of their condition, children with transfusion-dependent thalassemia should get blood transfusions once or twice monthly. They might have to remain in the hospital for the duration of the transfusion day, which would interfere with their social and academic life. Their self-esteem may suffer as a result of iron overload and the undesirable bronzed color. In addition, the risks associated with iron overload may become evident in the absence of chelation or as a result of patient noncompliance[(3)].

Chronic illness frequently interferes with growth and development. The chronic condition, and the expense of treatment, which includes frequent hospital stays, iron chelation, regular blood transfusions, general medical checkups, and surgery as needed, all contribute to concerns about physical, emotional, social, psychological, and behavioral appearance, interfering with the process of becoming independent and maintaining positive bonds with family and friends. Additionally, children's and adolescents' capacity to independently manage their illness is hampered by developmental issues [(4)]. During the academic years and the adolescent years, when kids are looking for independence, the disease's drawbacks in many areas of life become apparent. It has been connected to a psychosocial aspect and a significant detrimental effect on areas of school functioning because of the potential for physical deformity, growth retardation, and delayed puberty, as well as the difficulty of management (such as regular transfusion and time-consuming iron chelation treatment) [(5)].

It is necessary to evaluate the psychosocial effects of thalassemia to create informational guidelines for support and counseling programs to optimize coping with the disorder. Thalassemic patients and their families have experienced improved survival due to a high level of social integration, acceptance, and self-esteem, along with appropriate medical care and psychosocial support [(6).]

PATIENT AND METHODS

This is a case-control study that was conducted on 42 children, and adolescents with transfusion-dependent beta-thalassemia major and 42 healthy controls. They were recruited from Hematology Unit, Children's Hospital, Zagazig University, during the period from January 2022 to June 2022.

The patients were divided into two groups: 42 children and adolescents with beta-thalassemia major and

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42 healthy, age- and gender-matched children and adolescents.

The study included Patients with beta-thalassemia major, ages 6 to 18, who received regular blood transfusions. Legal guardians who were unable or unwilling to provide informed consent, age less than 6 years or more than 18 years, Patients, with beta-thalassemia who had any acute condition that made it difficult for them to respond to the questionnaire, such as acute heart failure or acute, and those with beta-thalassemia who had any associated chronic condition that wasn't connected to thalassemia or its complications, were excluded from the study.

Methods:

The following procedures were applied to all patients:

I. History taking:

It was intended for a structured questionnaire to collect the following information:

a) Information about your name, age, and gender.
b) Socioeconomic status (parents' educational backgrounds, their divorce, the number of children in the family, the number of siblings who have thalassemia, and the monthly family income).
c) Age at onset of beta-thalassemia.
d) Duration of disease.
e) Age at first blood transfusion, annual blood transfusion volume and frequency calculated by weight, and chelation therapy type, dosage, and duration.
f) History that is suggestive of any neurological disease or neurocognitive dysfunction.
g) Family past history.

II-Thorough clinical examination with particular emphasis on:

a) Chronological age which was revised from patient files and birth certificates.
b) Body mass index (BMI) calculations and anthropometric measurements, which include height and weight, are plotted on percentile lines for age and sex following Egyptian growth charts. BMI is determined by taking the ratio of weight in kilograms to height in square meters (kg/m^2)
c) Mongolid facies and abnormal colors: pallor and Jaundice.
d) Puberty was classified according to Tanner's stages.
e) A full neurological examination.

III. Psychological assessment using a questionnaire by the Arabic version of (CBCL/6-18) Child Behavior Checklist:

The Child Behavior Checklist (CBCL/6-18) is used to detect behavioral and emotional issues in kids and teenagers aged 6 to 18, and each parent's information on their child's behavior is gathered. It has 113 questions and is graded on a scale of 0 (absent), 1 (occurs occasionally), and 2 (occurs frequently). The test must be given in between 25 and 30 minutes.

Eight constructs or syndromes that deal with different aspects of behavior are evaluated by this instrument. This also allows the examination of two broad syndromes: internalizing problems (social withdrawal, somatic complaints, and anxiety, depression) and externalizing problems (delinquent behavior and aggressive behavior). Raw scores can be converted into age-standardized scores (T scores with a mean of 50 and a standard deviation of 10). Scores are interpreted as follows: For total problems, externalizing problems, and internalizing problems: T scores less than 60 are considered in the normal range. 60-63 represent borderline scores. Scores greater than 63 are considered in the clinical range [7].

Ethics approval:

The protocol for this study was approved by both the Institutional Review Board [IRB] and the local ethics committee at Zagazig University's Faculty of Medicine.

Statistical analysis

The information was analyzed using SPSS software (USA). The mean, standard deviation, or percentage are used to represent the parametric data. The statistical comparisons were performed using the independent student's t-test for continuous data and the Fischer exact test for categorical data. The relationship between the variables was evaluated using Spearman's correlation score test (2- tailed).

RESULTS

Table 1: Demographic data of the studied groups

	Cases (n=42)	Controls (n=42)	Test of Significance
Age (years)	10.5 ± 3.6 (6-18)	10.7 ± 3.4 (6-18)	**t= -0.27, P= 0.78**
Sex			**Fischer exact= 0.03**
Male	20 (47.6%)	19 (45.2%)	**P=1**
Female	22 (52.4%)	23 (54.8%)	
Weight	28.6 ± 10.3 (17-55)	33.1 ± 11.8 (18-60)	**t= -1.8, P= 0.07**
Height	126.6 ± 14.1 (100-158)	138.1 ± 16.5 (108-161)	**t= -3.3, P= 0.001***
Child Education			**Fischer exact= 3.5**
Elementary education	29 (69%)	22 (52.4%)	**P=0.189**
Secondary education	7 (16.6%)	7 (16.6%)	
Lower secondary	6 (14.4%)	13 (31%)	
Mother Education			**Fischer exact= 1.5**
Not Educated	14 (33%)	8 (19%)	**P=0.21**
Educated	28 (67%)	34 (81%)	
Father Education			**Fischer exact= 9.7**
Not Educated	16 (38%)	3 (7.2%)	**P=0.001***
Educated	26 (62%)	39 (92.8%)	
Marital status of the mother			**Fischer exact= 0.51**
Married	40 (95.2%)	42 (100%)	**P=0.49**
Father died	2 (4.8%)	0 (0%)	
Family size	4.8 ± 0.67 (3-6)	5.1 ± 1.1 (3-7)	**t= -1.1, P= 0.25**
Economic status			**Fischer exact= 8.4**
Low	12 (28.5%)	3 (7.1%)	**P=0.01**
Middle	30 (71.5%)	36 (85.7%)	
Moderate	0 (0%)	1 (2.4%)	
High	0 (0%)	2 (4.8%)	

Table 1 showed that there was no significant difference between the two groups regarding demographic data except for the father's education and economic status. Also, there was a significant difference regarding height which was shorter in cases than in the control group.

Table (2): Psychosocial grades among the studied groups

Anxiety depression	Cases (n=42)	Controls (n=42)	Test of Significance
Normal	13 (30.9%)	38 (90.4%)	Fischer exact=32.3 P<0.001*
Borderline	14 (33.3%)	2 (4.8%)	
Clinical	15 (35.8%)	2 (4.8)	
Withdrawn depressed			
Normal	14 (33.3%)	37 (88%)	Fischer exact=29.3 P<0.001*
Borderline	7 (16.6%)	3 (7.2%)	
Clinical	21 (50.1%)	2 (4.8%)	
Somatic complaints			
Normal	1 (2.3%)	37 (88%)	Fischer exact=82.7 P<0.001*
Borderline	1 (2.3%)	3 (7.2%)	
Clinical	40 (95.4%)	2 (4.8%)	
Social problems			
Normal	12 (28.4%)	37 (88%)	Fischer exact=31.7 P<0.001*
Borderline	15 (35.8%)	2 (4.8%)	
Clinical	15 (35.8%)	3 (7.2%)	
Thought problems			
Normal	35 (83.3%)	42 (100%)	Fischer exact=6.9 P=0.01*
Borderline	3 (7.2%)	0 (0%)	
Clinical	4 (9.5%)	0 (0%)	
Attention problems			
Normal	12 (28.5%)	37 (88%)	Fischer exact=31.7 P<0.001*
Borderline	10 (23.8%)	2 (4.8%)	
Clinical	20 (47.7%)	3 (7.2%)	
Rule breaking problems			
Normal	33 (78.5%)	38 (90.4%)	Fischer exact=2.3 P=0.38
Borderline	2 (4.8%)	1 (2.3%)	
Clinical	7 (16.7%)	3 (7.3%)	
Aggressive behavior			
Normal	22 (52.3%)	37 (88%)	Fischer exact=15.6 P<0.001*
Borderline	13 (31%)	1 (2.3%)	
Clinical	7 (16.7%)	4 (9.7%)	
Affective Disorders			
Normal	8 (19%)	37 (88%)	Fischer exact=42.6 P<0.001*
Borderline	5 (12%)	0 (0%)	
Clinical	29 (69%)	5 (12%)	
Anxiety problems			
Normal	4 (9.5%)	37 (88%)	Fischer exact=62.7 P<0.001*
Borderline	3 (7.2%)	2 (4.8%)	
Clinical	35 (83.3%)	3 (7.2%)	
Somatic problems			
Normal	16 (38%)	39 (92.8%)	Fischer exact=28.9 P<0.001*
Borderline	14 (33.3%)	1 (2.3%)_	
Clinical	12 (28.7%)	2 (4.9%)	
Attention deficit Hyper			
Normal	15 (35.7%)	38 (90.4%)	Fischer exact=28.3 P<0.001*
Borderline	13 (31%)	1 (2.3%)	
Clinical	14 (33.3%)	3 (7.3%)	

Anxiety depression	Cases (n=42)	Controls (n=42)	Test of Significance
Oppositional problems			
Normal	31 (73.8%)	37 (87.8%)	Fischer exact=3.3 P=0.02
Borderline	7 (16.6%)	2 (4.9%)	
Clinical	4 (9.6%)	3 (7.3%)	
Conduct problems			
Normal	26 (61.9%)	37 (87.8%)	Fischer exact=8.7 P=0.01*
Borderline	11 (26.1%)	2 (4.9%)	
Clinical	5 (12%)	3 (7.3%)	
Internalizing problems			
Normal	0 (0%)	32 (76%)	Fischer exact=74.1 P<0.001*
Borderline	1 (2.3%)	5 (12%)	
Clinical	41 (97.7%)	5 (12%)	
Externalizing problems			
Normal	12 (28.6%)	36 (85.7%)	Fischer exact=30.6 P<0.001*
Borderline	15 (35.7%)	1 (2.3%)	
Clinical	15(35.7%)	5 (12%)	
Total problems			
Normal	1 (2.3%)	32 (76.3%)	Fischer exact=57.2 P<0.001*
Borderline	6 (14.2%)	4 (9.5%)	
Clinical	35 (83.5%)	6 (14.2%)	

There was a significant difference between the two groups in terms of anxiety, depression, reticence, social problem, thought problems, attention problems, aggressive behavior, other mental health issues affective disorders, somatic problems, attention deficit hyper, externalizing problems grades that were clinical and borderline in cases more than in control group **(Table 2).**

Significant differences existed between the two groups regarding somatic complaints, anxiety problems, and internalizing problems grades that were clinical in cases more than in the control group. Significant differences existed between the two groups in terms to conduct problems grades that were borderline in cases more than in the control group **(Table 2).**

There was no significant difference between the two groups regarding rule-breaking problems, and oppositional problems **(Table 2).**

There was a significant difference between both groups regarding total problems grades that were clinical and borderline in cases more than in the control group **(Table 2).**

DISCUSSION

Except for the father's education and economic status, our findings revealed there were no observable demographic differences between the two groups. Additionally, there was a significant height difference, with cases being shorter than the control group**.**

This finding supports the findings of Elizabeth et al. [(8)] and Toumba et al. [(9)] who found that short stature was more common in thalassemia patients**.**

In the current study, 50% of cases had a history of the illness in their family, the majority of cases (57.1%) had one affected sibling, and the mean duration of disease was 8.9 ± 3.5 years, ranging from 5 to 17 years. The average time between blood transfusions was 10.8 ± 9.3 months, and the average frequency was every 20.1 ± 6.2 days. 62% of cases had severe mongoloid features, 40.6% had severe jaundice, and 100% received chelation therapy for an average of 7.6 ± 3.7 years**.**

In agreement with our findings, Ragb et al. [(1)] demonstrated that a total of 303 children aged 15-18 years were studied in their study on screening for thalassemia in Shebin El-Kom, Menoufia Governorate high school students, the majority of them (46.5%) presented in the age group from 15 to 16 years. The females outnumbered the males (62 vs. 38%, respectively). There is a positive history of consanguinity in 21.7% of the participants**.**

Regarding anxiety depression grades, there was a significant difference between both groups that was clinical (35.8%) and borderline (33.3%) in cases more than in the control group (4.8% and 4.8% respectively) P value <0.001. The findings demonstrated a significant difference between the two groups in terms of withdrawn depression grades that were clinical (50.1%) and borderline (16.6%) in cases more than the control group (4.8% and 7.2%, respectively) P value< 0.001**.**

Hongally et al. [(10)] found 34% of children had clinically significant, abnormal CBCL Internalization problem scores, indicating signs of Social withdrawal, somatic complaints, and anxiety/depression.

Furthermore, Poormansouri et al. [(11)] found that beta-thalassemia major patients had a high prevalence of

depression, anxiety, and moderate to severe stress, as well as a low quality of life.

In the current study, There were significant differences between the two groups in terms of clinical somatic complaint grades, with cases (95.4%) more than controls (4.8%). Additionally, there was a notable difference between both groups in terms of social problem grades that were clinical (35.8%) and borderline (35.8%) in cases more than the control group (7.2% and 4.8%) P value <0.001. Hakeem et al. [3] found that the mean physical score was significantly different between the two groups—36.9± 20.9 for patients and 78.4±5.5 for controls (p = 0.001). The emotional score for patients was 49.4± 17 while it was 74.3 ± 5.5 for controls; this difference was statistically significant (p = 0.001). The mean social score in the control group was 77 ± 13.9 and it was 47.2 ± 21.3 in the patient group with a significant difference (p = 0.001).

Our findings revealed a notable difference between the two groups in terms of thought problem grades that were clinical (9.5%) and borderline (7.2%) in cases more than the control group (0% and 0%, respectively) p=0.01.

This was consistent with the findings of ***Eghbali et al.*** [12], who discovered that when TM patients were compared to healthy children, they had significantly more thought problems (P=0.01).

Additionally, there was a notable difference between the two groups in terms of attention problems grades that were clinical (47.7%) and borderline (23.8%) in cases more than in the control group (7.2% and 4.8%, respectively) P value<0.001.

Elzaree *et al.* [5] found that the score of the attention domain was noticeably greater in children suffering from thalassemia (3.22) than in controls (3.02), p <0.000. Internalizing behavior was the most common, with 10% of patients exhibiting it.

Furthermore, **Eghbali *et al.*** [12] discovered that attention problems (P=0.03) were significantly higher in TM patients compared to healthy children.

The results showed that there was no significant difference between both groups regarding rule-breaking problems.

This was consistent with the findings of **Eghbali *et al.*** **[12]** who found no significant differences between cases and controls in rule-breaking problems (4.15 versus 3.05 respectively, P=0.20).

In the present study, there was a significant difference between both groups regarding aggressive behavior grades that were clinical (16.7%) and borderline (31%) in cases more than in the control group (9.7% and 2.3% respectively) P-value <0.001.

In agreement with our study, **Hongally *et al.*** [10] showed in the study results that a clinically significant, abnormal CBCL Externalization score was seen in 30% of cases, indicating delinquent and aggressive behavior symptoms**.**

Regarding affective disorders grades, there was a significant difference between both groups that was clinical (69%) and borderline (12%) in cases more than in the control group (12% and 0% respectively) P value <0.001.

This was consistent with **Almahmoud's** **[13]** who found that affective disorders, including anxiety disorders, are highly prevalent clinical conditions among patients with chronic illnesses such as thalassemia major, impacting patients' general functioning, worsening chronic illness management, and increasing morbidity. Risk-related cognitive tendencies affect the onset and development of affective disorders, including anxiety disorders, and internal, global, stable causal attributions constitute one of the main cognitive risk factors.

In the current study, there was a significant difference between the two groups in terms of clinical anxiety problem grades (83.3%) in cases more than in the control group (7.2%) P-value <0.001.

In agreement with our study**, Eghbali *et al.*** [12] found that anxiety was significantly higher in TM patients compared to healthy children.

In the current study, there was a significant difference between both groups regarding somatic problems grades that were clinical (28.7%) and borderline (33.3%) in cases more than in the control group (4.9% and 2.3%) P value <0.001.

Raman *et al.* [14] reported that TM patients had high somatic problems and anxiety, which are linked with decreased HRQoL in the physical and mental aspects of HRQoL, respectively.

In addition, In **Hosseini *et al.*** **[15]** study, somatic complaints, hypersensitivity to interactions, depression, anxiety, and psychosis were common psychological findings in thalassemia patients.

Our findings revealed a notable difference between the two groups regarding attention deficit hyper grades that were clinical (33.3%) and borderline (31%), in cases more than the control group (7.3% and 2.3%, respectively) P-value < 0.001.

In line with our findings, Eghbali et al. [12] reported that there were significant differences in attention problems between the two groups.

In the present study, there was a significant difference between both groups regarding oppositional problems grades that were borderline in cases (16.6%) more than in the control group (4.9%) p=0.02.

This was in agreement with **Patil *et al.*** [16]'s findings, which showed that in up to 80% of kids, Oppositional defiant disorder is a common psychological problem among thalassemia patients.

The current study found a significant difference between the two groups regarding conduct problem grades that were borderline (26.1%) in cases more than the control group (4.9%), p=0.01.

According to **Eghbali *et al*.** [12], the quality of life of 44 patients with TM (range: 6-18 years) revealed more anxiety-related symptoms, depression, and conduct problems than the control group.

There was a significant difference regarding internalizing clinical problem grades (97.7%) in cases more than in the control group (12%) P-value < 0.001.

This was consistent with the findings of **Ali *et al.*** [17] **and Raman *et al.*** [14] who reported that internalizing behavior such as mood changes, anxiety, irritability, and depression may develop as a result of peer victimization which can be overt forms (such as physical and verbal assault) and/or relational forms (social ostracism)

Regarding the grades of externalizing problems, there was a significant distinction between the clinical (35.7%) and borderline (35.7%) groups in cases more than the control group (12% and 2.3%, respectively) P-value <0.001.

In line with our findings, Bhattacharyya et al. [18] reported that externalizing behavior such as aggression, hyperactivity, and antisocialism may develop in children with thalassemia major as a reflection of a child's negative reactions to their disease, they don't listen to their parents when told to take their treatment or maintain an appropriate life style

In the current study, there was a significant difference in total problem grades that were clinical (83.5%) and borderline (14.2%) in cases more than (14.2%) and the control group (9.5%), with P-value < 0.001.

In agreement with our findings, Ghasemi et al. [19] found that children suffering from thalassemia had a higher prevalence of all psychosocial disorders than children in the control group.

In addition, **Shaligram *et al*.** [20] demonstrated that regarding the total psychological problems in the children with TM, the special symptoms and the physical illness with emotional problems factors in the CPMS incorporate elements relating to anxiety symptoms which along with emotional problems, particularly depression (62%), and conduct problems (49%) were the main findings. High scores were obtained on more than 1 factor by many children. The QOL of the children was affected by 29 (74%) on self-rating and 32 (82%) on proxy rating. The dimensions affected were Pain/discomfort (64%) followed by Anxiety/depression and Mobility (33% each), Usual activities (23%), and self-care (8%).

CONCLUSION

According to the results of our study, behavioral and psychological problems assessed by the Arabic version of the Child Behavior Check List, are common in patients with beta-thalassemia major. The increased risk of psychosocial problems in patients with thalassemia indicates the need for continuous psychosocial support to reduce their emotional distress, strengthen their coping competence, and improve their quality of life. Parents of thalassemia children also need psychological support during their children's treatment.

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