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Psychological Aspects in Children and Adolescents With Major Thalassemia: A Case-Control Study

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Background: Thalassemia is an inherited blood disease. It is a serious public health problem throughout the Mediterranean region, the Middle East and the Indian subcontinent, as well as in Southeast Asia.

Objectives: Thalassemia is an inherited blood disease. It is a serious public health problem. In this study we assessed psychological aspects in Iranian children and adolescents with thalassemia major.

Patients and Methods: In this case-control study sixty healthy subjects aged 7-18 years and Sixty Patients with confirmed diagnosis of major thalassemia were enrolled. After obtaining informed consent from parents of all participating thalassemia patients and healthycontrols, we assessed psychological aspects and quality of life by Pediatric Quality of LifeTM (PedsQL™), Strengths and Difficulties Questionnaires (SDQ), State and Trait Anxiety, Children's Depression Inventory (CDI).

Results: The results of this study indicate that there are significant changes in depression, anxiety, QOL and behavioral screening between children with thalassemia major compared with healthy subjects by means of both parents and children reports. According to the results, children with thalassemia major have more psychological problems than healthy ones. Patients with thalassemia have a lower QOL than their peers (P = 0.001), the rate of depression is higher in this group (P = 0.015), Also behavioral problems in these children are more than healthy subjects (P = 0.009).

Conclusions: We recommend appropriate treatment and counseling procedures in addition to specific treatment of thalassemia. According to the results we suggest to establish pediatric psychiatric clinics beside thalassemic clinics to cure psychological aspects of the disease.

Keywords: Adolescents; Children; Quality of Life; Thalassemia Major

1. Background

Thalassemia is an inherited blood disease. It is a serious public health problem throughout the Mediterranean region, the Middle East and the Indian subcontinent, as well as in Southeast Asia (1). Out of approximately 300 million carriers of this hemoglobin disorder worldwide (2). Among the Estern Mediterranean region, Iran is one of the major centers for the prevalance of Beta-thalassemia.It is estimated that there are between 2-3 million B-thalassemia carriers and 25,000 patients in Iran (3). Beta-thalassemia is a chronic and genetically determined hematological disorder characterized by severe hemolytic anemia as a result of deficient synthesis of β chains of the hemoglobin. The anemia demands frequent blood transfusions to maintain life, while hemosiderosis and other complications of the disease require a continuous and distressing treatment regimen that includes parenteral iron chelation treatment and regular medical supervision. Thalassemia is a chronic disease that presents a range of serious clinical and psychological challenges. The effects of thalassemia on physical health can lead to physical deformity, growth retardation, and delayed puberty (4-6). Its impact on physical appearance, e.g. bone deformities and short stature, also contributes to a poor self-image (5, 6). Severe complications such as heart failure, cardiac arrhythmia, liver disease, endocrine complications, and infections are common among thalassemia patients (7, 8). Despite the critical advances in the knowledge of the psychological assessment in chronic patients, very few studies are carried out to investigate correlation between psychological conditions and quality of life in Thalassemia major (TM) patients (9-11). As the mean age and life expectancy

of TM patients expands, psychosocial issues related to quality of life become an increasingly important focus of attention (12, 13). It is universally known that chronic diseases have a psychological implication, which in pediatric age has a great importance. Children with chronic physical illnesses exemplified by thalassemia are vulnerable to emotional and behavioral problems (14). The onset of symptoms, the rigors of treatment, and frequent absence from school make huge demands on the emotional and interpersonal resources of the children and their families. The emotional and cognitive needs of a child with thalassemia are patently different from those of the adolescents striving for independence and identity. Adults with thalassemia face problems related to career, finding partners, establishing a family (due to infertility) and waning social support as parents age. Thus each age group has problems unique to that stage of development. However, the increasing longevity of children with thalassemia has brought psychological problems to the fore. Various authors have reported that up to 80% of children with thalassemia are likely to have psychological problems e.g. oppositional defiant disorder, anxiety disorders and depression (15-17). Although children with all types of blood disorders are exposed to similar stressors, those with thalassemia are unique in that they have to attend hospital regularly for blood transfusions (18). Clemente et al. 2002, concluded that specific blood disorders have differential impact on affected children, resulting in higher rates of psychological disturbances in children with thalassemia (17). A Quality of Life (QOL) study in adolescents with thalassemia indicates that those with psychiatric symptoms had poorer QOL (5).

2. Objectives

There is a dearth of studies that address QOL across different age groups in children with thalassemia. In this study we aimed to assess psychological aspects and QOL in Iranian children and adolescents with thalassemia major compared with control group.

3. Patients and Methods

This is a Case-Control study. Sixty healthy subjects aged 7-18 years were also enrolled from pediatric clinics for routine checks, chronic diseases were ruled out in all of them. Sixty children and adolescents (aged 7-18 years) with confirmed diagnosis of major thalassemia were referred to Sarvar pediatric thalassemia clinic, Mashhad, Iran. The study was approved by the ethical committee on human research of Mashhad University of Medical Sciences. After obtaining informed consent from parents of all participating thalassemic patients and healthy controls, we assessed psychological aspects and quality of life by Pediatric Quality of LifeTM (PedsQL™), Strengths and Difficulties Questionnaires (SDQ), State and Trait Anxiety, Children's Depression Inventory (CDI).

3.1. Questionnaire Measures

3.1.1. Strengths and Difficulties Questionnaires (SDQ)

The SDQ is a brief questionnaire that can be administered to the parents and teachers of 4- to 16-year-olds and to 11- to 16-year-olds themselves (19-21). Besides covering common areas of emotional and behavioral difficulties, it also enquires whether the informant thinks that the child has a problem in these areas. The algorithm makes separate predictions for three groups of disorders, namely conduct-oppositional disorders, hyperactivity-inattention disorders, and anxiety-depressive disorders. Each is predicted to be unlikely, possible or probable. Predictions of these three groups of disorders are combined to generate an overall prediction about the presence or absence of any psychiatric disorder. A specificity of 95% (95% Cl 94.1-95.1%) and a sensitivity of 74% (59.7-66.9%) is identified in Iranian pediatric population (22).

3.1.2. Pediatric Quality of LifeTM (PedsQL™)

The Peds QLTM 4.0 questionnaire was used for four different age groups: 2-4, 5-7, 8-12 and 13-18 years of age, and included four different fields of children's function: physical function, emotional function, social function and school (and pre-school courses) function. PedsQLTM has children forms (for 5-7, 8-12, 13-18 year old children) which were filled by children, and parents' forms (for 2-4, 5-7, 8-12, 13-18 year old children) which were filled by their parents. Each question could get one of the five scores of 0 for "never" up to 4 for "almost always"; the total score was calculated by dividing the added score of different sections over the number of answered questions (7) and an ideal score was 100. PedsQLTM was translated to Persian language and had a validity value of more than 0.7 when filled by the patient or his/her parents. The test and its repetition showed a high reliability in parents' reports (0.68-0.79) and a medium to high reliability in children's reports (0.46-0.73) (23).

3.1.3. Children's Depression Inventory (CDI)

The Children's Depression Inventory (CDI) (24, 25) is a 27-item scale designed for use with children aged 8-14 years. Each item consists of three statements that describe the absence, presence, and severity of the symptom within the last 2 weeks. For each item, the child's score (0, I, or 2) is in the direction of the depression. The children read the items themselves or have the items read to them. The reliability and validity of the CDI are well established and norms for prepubertal children have been developed (25). The CDI has been shown to discriminate between depressed and nondepressed children (26, 27). Its internal reliability is high (27, 28).

3.1.4. Child State-Trait Anxiety Inventories (SATA)

This inventory, developed by Spielberger (29) has 2 sub-

scales, each composed of 20 multiple choice questions for state trait anxiety. Each item is scored as 0, 1, or 2 according to the severity of the symptom. State anxiety defines the experienced anxiety under certain conditions and at a certain time and changes according to external factors. On the other hand, trait anxiety defines the feelings of the individual in general and reflects the individual's general predisposition to anxiety. Its internal reliability is high (29).

3.2. Statistical Analysis

The collected data were analyzed using the SPSS program, version 16. The results were calculated in each group and compared between two groups. The Chi-square test and independent test were used to determine the difference between various variables, and the P-value was set as < 0.05 for significance.

4. Results

Sixty patients with thalassemia major and 60 healthy participants were enrolled in the study. Fifty six (46.67%) participants were females and 64 (53.33%) males. The mean scores of different subscales of SDQ, SATA and QOL are presented in Table 1. According to the results, no significant difference was observed in depression between patients with and without growth disorder in thalassemia major group (P = 0.56). In addition, there were no specific differences in anxiety, QOL and behavioral screening between patients with and without growth disorder in thalassemia major group. Tables 2 and 3 show the mean scores of depression in CDI. There is no significant difference between males and females regarding subscales of SDQ in thalassemic patients and healthy participants. No significant differences were observed in depression between different ages (children, 8-11 years and adolescents, 12-18 years) in thalassemic group (P = 0.56). Furthermore, there were no significant differences in anxiety and QOL between different ages in the group of thalassemia major. In Table 4, thalassemia and healthy subjects are compared by means of depression, anxiety and QOL (P = 0.015, P = 0.034, P = 0.001, respectively). Also there were significant differences in behavioral problems (SDQ) including emotional, conduct, hyperactivity, peer relationship, social and all states between two groups (P = 0.01, P = 0.01, P = 0.03, P = 0.03, P = 0.02, P = 0.009, respectively). Table 5 shows a significant difference in QOL between major thalassemia and healthy groups (P = 0.04). In addition, significant differences were seen in behavioral problems (SDQ) including emotional, conduct, hyperactivity, peer relationship, social and all states between two groups (P = 0.039, P < 0.001, P = 0.03, P = 0.01, P = 0.02, P < 0.001, respectively). Table 6 shows that there was a significant difference in QOL between children and parents' sight in major thalassemia group (P < 0.001). Also significant changes were seen in some of behavioral screenings including emotional, social and all states between children and parents' sight in major thalassemia group (P = 0.001, P < 0.001, P < 0.001, respectively). In contrast, no significant differences were seen in other behavioral screenings including conduct, hyperactivity, peer relationship between children and parents' viewpoints in major thalassemia group (P = 0.28, P = 0.91, P = 0.39, respectively).

Table 1. Demographic Characteristics of Patients with Thalassema Major [a]

Variable	Major Thalassemia Group	Control Group
Age, y	13.18 (3.69)	13.75 (3.22)
Gender		
Male	33 (55)	31 (51.7)
Female	27 (45)	29 (48.3)
Physical disorders		
Diabetes	7 (11.7)	
Heart failure	4 (6.7)	
Skin discoloration	28 (46.7)	
Face changes	40 (66.7)	
Growth disorder	31 (51.6)	
Desferal injection	52 (86.7)	
Age at the first desferal injection	1.88 (1.50)	
Min	1	
Max	7	
Number of blood transfusions received during a year	17.65 (3.28)	
Min	13	
Max	26	

[a] Data are presented as No. (%) or No.

Table 2. Psychological Problems Between Male and Female in Group With Thalassemia Major From Viewpoint of Children [a,b]

Variable	Male	Female	P Value
Depression	8 (24.2)	8 (29.6)	0.77
Anxiety			0.571
Low state, low trait	5 (15.2)	3 (11.1)	
High state, low trait	20 (60.6)	13 (48.1)	
Low state, high trait	2 (6.1)	2 (7.4)	
High state, high trait	6 (18.2)	9 (33.3)	
QOL			0.777
Low	2 (6.1)	2 (7.4)	
Medium	7 (21.2)	3 (11.1)	
Good	11 (33.3)	10 (37)	
Perfect	13 (39.4)	12 (44.4)	
SDQ			
Emotional			0.129
Low	1 (4.5)	1 (5)	
Medium	30 (91)	20 (75)	
Good	1 (4.5)	5 (20)	
Conduct			0.28
Low	4 (13.6)	3 (10)	
Medium	13 (40.9)	18 (65)	
Good	15 (45.5)	7 (25)	
Hyperactivity			0.051
Low	0	0	
Medium	30 (90.9)	19 (70)	
Good	3 (9.1)	8 (30)	
Peer relationship			0.589
Low	3 (9.1)	1 (5)	
Medium	25 (77.3)	20 (75)	
Good	4 (13.6)	5 (20)	
Social			0.224
Low	0	0	
Medium	31 (95.5)	24 (90)	
Good	1 (4.5)	3 (10)	
All states			0.14
Low	4 (13.6)	11 (40)	
Medium	15 (45.5)	9 (35)	
Good	13 (40.9)	7(25)	

[a] Abbreviations: QOF, Quality of Life; SDQ, strengths and difficulties questionnaires.
[b] Data are presented as No. (%).

Table 3. Psychological Problems Between Male and Female in Healthy Subjects From Children Viewpoint [a,b]

Variable Variable	Male	Female	P Value
Depression	1 (3.2)	4 (13.8)	0.18
Anxiety			0.294
Low state, low trait	5 (16.1)	11 (37.9)	
High state, low trait	18 (58.1)	13 (44.8)	
Low state, high trait	2 (6.5)	1 (3.4)	
High state, high trait	6 (19.4)	4 (13.8)	
QOL			0.39
Low	0	0	
Medium	0	1 (4.3)	
Good	11 (35.5)	7 (24.1)	
Perfect	20 (64.5)	21 (72.4)	
SDQ			1
Emotional			
Low	0	0	
Medium	30 (95.7)	27 (92)	
Good	1 (4.3)	2 (8)	
Conduct			0.281
Low	0	2 (8)	
Medium	26 (82.6)	23 (80)	
Good	5 (17.4)	3 (12)	
Hyperactivity			0.18
Low	0	0	
Medium	26 (82.6)	28 (96)	
Good	5 (17.4)	1 (4)	
Peer relationship			0.447
Low	1 (4.3)	0	
Medium	27 (87)	24 (84)	
Good	3 (8.7)	5 (16)	
Social			0.35
Low	0	0	
Medium	30 (95.7)	24 (84)	
Good	1 (4.3)	5 (16)	
All states			0.73
Low	1 (4.3)	2 (8)	
Medium	23 (73.9)	19 (64)	
Good	7 (21.7)	8 (28)	

[a] Abbreviations: QOF, Quality of Life; SDQ, strengths and difficulties questionnaires.
[b] Data are presented as No. (%).

Table 4. Psychological Problems Between Two Groups From Children Viewpoint [a,b]

Variable	Major Thalassemia Group	Healthy Group	P Value
Depression	8 (13.33)	3 (4.17)	0.015
Anxiety			0.034
Low state, low trait	4 (6.67)	9 (15)	
High state, low trait	17 (27.50)	12 (20)	
Low state, high trait	2 (3.33)	5 (7.50)	
High state, high trait	8 (12.50)	5 (7.50)	
QOL			0.001
Low	2 (3.33)	0	
Medium	5 (8.33)	1 (0.83)	
Good	11 (17.50)	9 (15)	
Perfect	13 (20.83)	21 (34.17)	
SDQ			
Emotional			0.01
Low	10 (16.7)	0	
Medium	44 (73.2)	56 (93.7)	
Good	4 (7.1)	4 (6.2)	
Conduct			0.01
Low	7 (11.9)	3 (4.2)	
Medium	31 (52.4)	49 (81.2)	
Good	21 (35.7)	9 (14.6)	
Hyperactivity			0.03
Low	5.7 (9.5)	0	
Medium	43 (71.4)	54 (89.6)	
Good	11 (19)	6 (10.4)	
Peer relationship			0.03
Low	10 (16.7)	1 (2.1)	
Medium	40 (66.7)	51 (85.4)	
Good	10 (16.7)	7 (12.5)	
Social			0.02
Low	9 (14.3)	0	
Medium	47 (78.6)	54 (89.6)	
Good	4 (7.1)	6 (10.4)	
All states			0.009
Low	16 (26.2)	4 (6.2)	
Medium	24 (40.5)	41 (68.6)	
Good	20 (33.3)	15 (25)	

[a] Abbreviations: QOF, Quality of Life; SDQ, strengths and difficulties questionnaires.
[b] Data are presented as No. (%).

Table 5. Psychological Problems Between Two Groups From Parents' Viewpoint [a,b]

Variable	Major Thalassemia Group	Healthy Group	P Value
QOL			0.04
Low	2 (3.3)	0	
Medium	10 (16.7)	3 (5)	
Good	19 (31.7)	16 (26.7)	
Perfect	29 (48.3)	41 (68.3)	
SDQ			
Emotional			0.039
Low	15 (25)	6 (10)	
Medium	39 (65)	41 (68.3)	
Good	6 (10)	13 (21.7)	
Conduct			< 0.001
Low	19 (31.7)	5 (8.3)	
Medium	23 (38.3)	45 (75.3)	
Good	18 (30)	10 (16.7)	
Hyperactivity			0.03
Low	10 (16.7)	2 (3.3)	
Medium	37 (61.7)	47 (78.3)	
Good	13 (21.7)	11 (18.3)	
Peer relationship			0.01
Low	7 (11.7)	0	
Medium	43 (71.7)	52 (86.7)	
Good	10 (16.7)	8 (13.3)	
Social			0.02
Low	9 (15)	1 (1.7)	
Medium	46 (76.7)	51 (85)	
Good	5 (8.3)	8 (13.3)	
All states			< 0.001
Low	22 (36.7)	4 (6.9)	
Medium	18 (30)	42 (70.7)	
Good	20 (33.3)	13 (22.4)	

[a] Abbreviations: QOF, Quality of Life; SDQ, strengths and difficulties questionnaires.
[b] Data are presented as No. (%).

Table 6. Psychological Problems Between Children and Parents' Viewpoints in Major Thalassemia Group [a,b]

Variable	Children	Parents	P Value
QOL			< 0.001
Low	2 (3.33)	8(12.50)	
Medium	5 (8.33)	20 (32.50)	
Good	11 (17.50)	3 (5)	
Perfect	13 (20.83)	0	
SDQ			0.001
Emotional			
Low	10 (16.7)	19 (31.7)	
Medium	46 (76.2)	23 (38.3)	
Good	4 (7.1)	18 (30)	
Conduct			0.28
Low	7 (11.9)	10 (16.7)	
Medium	31 (52.4)	37 (61.7)	
Good	21 (35.7)	13 (21.7)	
Hyperactivity			0.91
Low	6 (9.5)	7 (11.7)	
Medium	43 (71.5)	43 (71.7)	
Good	11 (19)	10 (16.7)	
Peer relationship			0.39
Low	10 (16.7)	9 (15)	
Medium	40 (66.7)	46 (76.7)	
Good	10 (16.7)	5 (8.3)	
Social			< 0.001
Low	9 (14.3)	22 (36.7)	
Medium	47 (78.6)	18 (30)	
Good	4 (7.1)	20 (33.3)	
All states			< 0.001
Low	16 (26.2)	4 (6.7)	
Medium	27 (45)	47 (78.3)	
Good	20 (33.3)	9 (15)	

[a] Abbreviations: QOF, Quality of Life; SDQ, strengths and difficulties questionnaires.
[b] Data are presented as No. (%).

5. Discussion

The results of this study indicate that there are significant differences in depression, anxiety and QOL and behavioral screening between children with thalassemia major compared with healthy subjects by means of both parents and children reports. According to the results, children with thalassemia major have more psychological problems than healthy ones. Also parents assessed not only their children's quality of life but also emotional and social behavior significantly worse than their children ($P < 0.001$). Hadi et al. (30) observed that QOL in terms of physical health and its related aspects was lower in patients with thalassemia major than in control group. Also Shaligram et al. (31) foun that in thalassemia major group 74% had a low quality of life. The results of these two studies are similar to our findings. In an other study that was conducted by Masera et al. (32), 80 percent of children with thalassemia major had at least one psychiatric disorder. In the study conducted by Khani et al. (33) in Mazandaran province, Iran, 64.9% of patients with thalassemia major had no psychological problems. The result of our study indicate that patients with thalassemia had a high risk of psychiatric disorders and therefore may require psychological counseling. Depression is one of the most common psychiatric disorders in patients with thalassemia major. According to our results 26.7% of patients were depressed, this was significantly more than in control group. In the study by Ghaffari Saravi et al. (34) in Sari city in Iran depression was assessed in 165 children with thalassemia. According to the results of this study, depression in patients with thalassemia major (14%) was significantly higher (5,5%) than in the control group. The rate of depressive symptoms in our study is higher than that of Ghaffari Saravi et al. (34). In the Shaligram et al. (31) study depressive symptoms were reported in 62% of thalassemia patients that is the highest rate reported in recent studies. In a other study by Cakaloz et al. (35) on 25 thalassemic patients the psychiatric diagnosis was significantly higher (55.0%) in the children with TM as compared to the control group (14.7%). The thalassemic children showed an anxiety disorder frequency of 30.0% and a depressive disorder frequency of 15.0%. This study had a small sample size compared to our study. In the study of Ghanizadeh et al. (36) on 110 children and adolescents with TM, about 49% suffered from depressive symptoms which is more than our results (26.7%). According to our results the state of anxiety in children with TM was significantly higher than in healthy children. In our study low trait, high state and high trait, high state were higher in TM children which Indicates the higher stress level in patients with thalassemia. Similarly, Aydin et al. (37) found that hopelessness and trait-anxiety score were significantly higher in patients with thalassemia major than the in control group. Also in a study by Cakaloz et al. (35) children with thalassemia showed greater Anxiety disorder (30%). In our study, overall behavioral problems were seen more in children with thalassemia than in control group. Although the rate of conduct problems was lower in thalassemic group. In contrst to Shaligram et al. (31) study that have shown conduct disorder to be high (49%) in children with thalassemia, our findings did not confirm it. We compared QOL from the viewpoints of children and their parents. Parents assessed their children's quality of life significantly lower than their children themselves. Similarly, Alavi et al. (38) observed too, that parents assessed their children's quality of life significantly lower than their children. In our study, there were no significant differences in depression between male and female children with TM; anxiety symptoms were higher in female group. In addition, our female group had a higher QOL than males. Mikelli and Tsiantis (5) in 2004 showed that girls with TM had a lower depression and a higher quality of life than the boys with TM. They reported lower levels of depression Compared to the present study. Alavi (38) found that QOL in girls was worse than in boys just in physical aspects. It can be concluded that patients with thalassemia due to disease progress and its problems have a lower QOL than their peers and the rate of depression is higher in this group. Also behavioral problems in these children are in a lower level than in healthy subjects. We recommend appropriate treatment and counseling procedures in addition to specific treatment of thalassemia. According to the results we suggest to establish pediatric psychiatric clinics in beside thalassemic clinics to cure psychological aspects of the disease.

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