DEPRESSION, ANXIETY AND QUALITY OF LIFE IN ADOLESCENTS WITH TRANSFUSION-DEPENDENT THALASSEMIA

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Abstract

Background: Thalassemia is a common health problem in Mediterranean region including Egypt. Repeated regular blood transfusion with chelation therapy represented the gold standard treatment. However, associated psychiatric disorders could play a role in the pathogenesis and response to treatment.

The aim of the work: To assess depression, anxiety and quality of life among adolescents with thalassemia.

Methodology: This cohort study included 150 thalassemic adolescents and 150 healthy age and sex matched controls. Each patient was submitted to full history taking, detailed clinical examination and laboratory workup. Then, psychiatric disorders were assessed by Hamilton depression rating scale (HAM-D)**,** Hamilton Anxiety Rating Scale (HAM-A) and McGill quality of life questionnaires.

Results: The age ranged between 13 and 18 years, with no significant difference between the study and control groups. Males represented 48.0% and 43.3% of the study and control groups respectively, p >0.05). The majority of patients in thalassemia group diagnosed at their first year (43.3%). Patients in the thalassemia group had significantly lower weight and height. However, consanguinity was significantly higher among the study than the control group (40.7% vs 21.3%). RBCs indices and count were significantly lower, while hemoglobin F was significantly higher in the thalassemia than the control group. The mean HAM-D and HAM-A score were significantly higher in the study than the control group (15.12±3.0, 17.42±5.63 vs 10.94±3.07 and 12.29±5.25, respectively), while McGill QoL score significantly reduced in the study than the control group (5.44±1.11 vs 6.56±0.89, p < 0.001). HAM-D and HAM-A score inversely correlated with quality of life score. And only HAM-A inversely correlated with hemoglobin F in the study group.

Conclusion: Transfusion dependent-thalassemia is associated with increased psychiatric (mainly anxiety and depression) and lower quality of life. Interventional programs are recommended for future plans of treatment.

Keywords: Thalassemia; Anxiety; Depression; Quality of Life; Adolescents

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INTRODUCTION

Thalassemia is a common chronic genetic blood disease. It is due to a genetic deficiency of one or more globin polypeptide chains synthesis. Clinically, thalassemia presented by severe chronic anemia, growth restriction, organomegaly (mainly hepatosplenomegaly) and variable bone deformi- ties. It had a substantial burden on all aspects of patient's life [(1,2)]. Thalassemia is a major health problem, with different distribution among worldwide countries. For example, 1.5% of world populations (e.g., 0.5% in Myanmar to 12.8% in Malaysia) are carriers. However, significant variations occur in different geographic regions irrespective of the well-known overall prevalence (of carriers plus those with overt disease). For example, it ranges from 1.25% to 1.66% in India to 2.21% in China, and reached up to 9.0% in Egypt [(3,4)].

In addition to its burden on the patients and their families, thalassemia had a public health impact due to the treatment cost due to frequent admissions, regular follow up, blood transfusion, and iron chelation [(5,6)].

With improved medical treatment options, the life span of thalassemic patients is increasing.

However, this prolongation of therapeutic period is associated with different effects of the patient's quality of life and other social aspects. The chronic nature of the disease could be associated with an increased risk of the development of different psychiatric comorbid conditions [(7)].

The adolescent represents a special transition phase between late childhood and early adulthood, with different changes. Thalassemic patients experience negative effects of the disease on their physical appearance, as well as, their academic achievement and social interactions. This could negatively affect their quality of life and psychiatric disorders are likely to develop [(8,9)].

The psychiatric assessment in patients with chronic diseases witnessed critical advances in the last decades. However, few studies addressed the psychological conditions and quality of life in adolescents with thalassemia. Thus, we aimed to assess the psychiatric disorders and social problems associated with thalassemia among adolescents.

PATIENTS AND METHODS

This was a cohort study. It included 150 thalassemic children (as the study group) and other 150 healthy, age and sex matched children (as a control group). The study was completed between June 2021 and June 2022. Participants were selected from the Pediatrics Department and Psychiatric Outpatient Clinic, New Damietta University Hospital, Al-Azhar University, Egypt.

In the study group, participants were included if they have a confirmed diagnosis of thalassemia with regular blood transfusion and chelating agent therapy. In addition, their aged ranged between 13 and 18 years, with no family or past history of psychiatric disorders. Both participant assent and their guardian informed written consent were obtained before participation and after full explanation of the study protocol. The study completed in accordance with the Helsinki declaration codes of research conduct and reporting. The study protocol was reviewed and approved the Research Ethics Committee of Damietta Faculty of Medicine, Al-Azhar University, Damietta, Egypt.

If the participants or their guardians refused to participate, under treatment for current psychiatric disorders, or had any neurological or other chronic medical conditions, were excluded from the study.

Details of their physical condition were collected (e.g., age at diagnosis of thalassemia, and frequency of blood transfusion, etc.). Detailed clinical examination and Laboraty workup were also performed. The workup included complete blood count, serum ferritin, hemoglobin electrophoresis, tests for liver and kidney functions, calcium, phosphorus and alkaline phosphatase.

The psychiatric evaluation was done by the Hamilton depression rating scale (HAM-D)[(10,11)], and Hamilton Anxiety Rating Scale (HAM-A) [(12)]. The quality of life was assessed by the McGill quality of life questionnaire [(13)].

For HAM-D, participants, helped by their parents filled the questionnaire after proper instruction and semi-structured clinical interview (this is a midway between structured with strict questions and unstructured clinical interview. It started by using a pre-prepared guide for questions and the physician ask them in different ways for different participants. Open ended questions are the role). HAM-D is a 17 items questionnaire which takes about 20 minutes to be completed. It assess the symptoms of depression over the past week. Score between 10 and 13 indicate mild, 14-17 mild to moderate, and > 17 moderate to severe depression [(10,11)]. The Hamilton Anxiety Rating Scale (HAM-A) consists of 14 items, measures both psychic anxiety (mental agitation and psychological distress) and somatic anxiety (physical complaints related to anxiety). Each item is scored on a scale of 0 (not present) to 4 (severe), with a total score range of 0–56, where scores <17 indicates mild severity, 18–24 mild to moderate severity and 25–30 moderate to severe [(12)]. The McGill quality of life questionnaire was designed to be self-administered. However, it can be read aloud to the patient by a research team member. It takes about 15 minutes to be completed. Each item score from 0 to 10, and higher scores indicate better quality of life [(13)].

Data analysis:

The data was anonymized and fed to personal computer and analyzed by the Statistical Package for the Social Sciences (SPSS, Chicago, IL; USA) software v. 18. For quantitative normally distributed data, the means and standard deviation (SD) were calculated. Otherwise, median and interquartile range were calculated. On the other side, qualitative data were presented by the relative frequencies and percentages (calculated from each group). Quantitative data were

compared by Student's "t" test. Qualitative variables were compared with Chi square or Fisher's exact tests as appropriate. P value < 0.05 was considered statistically significant.

RESULTS

In the current work, participant age ranged between 13 and 18 years, with no significant difference between the study and the control group. In addition, no significant difference was observed between the study and control group regarding gender (males represented 48.0% and 43.3% of the study and control groups respectively). The majority of participants in thalassemia group diagnosed at their first year (43.3%) followed by the third and second years (27.3% and 20.7% respectively). The thalassemia (study) group had significantly lower weight and height than the control group. The consanguinity between father and mother was significantly higher among the study than the control group (40.7% vs 21.3%) (Table 1).

As regard to initial presentation of participants in the study group, all were presented with pallor, 50.0% with dark urine, 74.7% with jaundice, 50.0% with abdominal enlargement; and all under regular blood transfusion. The frequency of blood transfusion was every two weeks in 20.0%, every three weeks in 10.0% and every month in 70.0%. The first transfusion was performed as the same year of diagnosis.

Laboratory investigations are presented in table (2). The results showed that, thalassemia group had significantly lower RBCs, hemoglobin, and other RBCs indices than the control group. However, no significant difference was observed regarding white blood cell and platelet count. In addition, there was significant increase of hemoglobin F, phosphate and alkaline phosphatase and significant reduction of calcium in the study than the control group.

The Hamilton Depression and anxiety scores were significantly higher in the study than the control group, while the McGill quality of life score was significantly lower among study than the control group (Table 3).

Hamilton depression score proportionately and significantly correlated with Hamilton anxiety score but inversely with McGill quality of life score. In addition, Hamilton Anxiety score inversely and significantly correlated with McGill quality of life score. In addition, Hamilton Anxiety score inversely and significantly correlated with hemoglobin F (mild correlation) (Table 4).

Table (1): Patient characteristics and age of diagnosis of thalassemia in the study group

Variable	Measures	Study group	Control group	Test	P value
Age (years)	Mean±SD; min.-max.	15.37±0.93; 13-18	15.41±0.80; 14-17	0.40	0.69
Age at diagnosis (year) (n,%)	First	65 (43.3%)			
	Second	31 (20.7%)			
	Third	41 (27.3%)			
	Fourth	10 (6.7%)			
	Fifth	3 (2.0%)			
Sex (n,%)	Male	72(48.0%)	65(43.3%)	0.65	0.41
	Female	78(52.0%)	85 (56.7%)		
Mother-father Consanguinity	Positive	61 (40.7%)	32 (21.3%)	***13.10***	***<0.001****
	Negative	89(59.3%)	118 (78.7%)		
Weight (kg)	Mean±SD	57.93±3.58	61.74±3.09	***9.84***	***<0.001****
Height (cm)	Mean ±SD	146.15±3.34	151.62±3.41	***14.02***	***< 0.001****

SD: Standard deviation; Min.: minimum, Max.: Maximum; * indicate significant differences

Table (2): Main laboratory findings at the time of inclusion in the study

		Study	Control	Test	P
CBC	RBCsx10^6/ml	3.20±0.37	4.09±0.31	22.11	**<0.001***
	Hemoglobin (gm/dl)	8.01±0.92	11.10±0.70	32.81	**<0.001***
	HCT %	25.22±2.95	35.30±2.23	33.30	**<0.001***
	MCV	71.74±8.42	87.25±4.61	19.77	**<0.001***
	MCH	23.12±2.71	28.90±2.02	20.90	**<0.001***
	MCHC	32.37±3.80	40.81±2.89	21.60	**<0.001***
	WBCs x 10^3	8.65±1.38	8.42±1.18	1.54	0.12
	Platelets x 10^3	356.42±31.23	367.44±29.98	0.57	0.55
Hemoglobin electrophoresis	HA1	75.48±5.14	95.62±0.97	***4.70***	***<0.001****
	HA2	3.31±1.03	3.16±0.94	1.34	0.18
	HF	21.21±5.11	1.21±0.23	***47.83***	***<0.001****

Calcium (mg/dl)	9.00±0.42	10.40±0.33	***32.01***	***<0.001****
Phosphorus (mg/dl)	4.95±0.56	3.97±0.57	***14.74***	***<0.001****
Alkaline phosphatase (IU/L)	153.87±13.20	136.20±21.74	***8.51***	***<0.001****

CBC: Complete blood count: RBCs: Red blood cells; HCT: hematocrit; MCV: mean cell volume: MCH: mean cell hemoglobin; MCHC: mean cell hemoglobin concentration; WBCs: White blood cells; HA: hemoglobin Alpha; HF: Fetal hemoglobin; * indicate significant differences

Table (3): Psychiatric disorders among the study and control groups

		Study	Control	Test	P
Depression	None	0 (0.0%)	44(29.3%)	82.03	<0.001*
	Mild	67 (44.7%)	73 (48.7%)		
	Mild to moderate	48(32.0%)	33 (22.0%)		
	Moderate to severe	35(23.3%)	0 (0.0%)		
	HAM- D (Mean±SD)	15.12±3.00	10.94±3.07	11.91	<0.001*
Anxiety	None	0 (0.0%)	16 (10.7%)	51.94	<0.001*
	Mild	84 (56.0%)	114 (76.0%)		
	Mild to moderate	43 (28.7%)	20 (13.3%)		
	Moderate to severe	23 (15.3%)	0 (0.0%)		
	HAM-A (mean±SD)	17.42±5.63	12.29±5.25	8.16	<0.001*
McGill Quality of Life score		5.44±1.11	6.56±0.89	9.60	<0.001*

* indicate significant differences

Table (4): Correlation between McGill quality of life, Hamilton depression, anxiety scales and other variables

	HAM-D		HAM-A		MQoL	
	r	p	r	p	r	p
Age	0.021	0.795	0.012	0.888	0.041	0.617
Age at diagnosis	0.013	0.873	0.097	0.237	-0.040	0.625
Weight	-0.006	0.941	-0.050	0.543	0.100	0.224
Height	-0.038	0.645	-0.072	0.383	0.108	0.189
RBCs	-0.085	0.302	0.008	0.924	0.003	0.975
Hb	-0.009	0.916	0.044	0.589	0.001	1.000
HCT	-0.031	0.705	0.044	0.597	-0.013	0.872
MCV	-0.085	0.301	0.010	0.901	0.002	0.978
MCH	-0.086	0.293	0.005	0.950	0.006	0.944
MCHC	-0.086	0.293	0.005	0.950	0.006	0.944
WBCs	-0.062	0.450	-0.006	0.939	-0.073	0.373
Platelets	0.149	0.069	0.018	0.830	-0.026	0.749
HA1	0.114	0.165	0.187*	0.022	-0.047	0.564
HA2	-0.073	0.374	-0.022	0.791	-0.062	0.451
HF	-0.100	0.224	**-0.184***	**0.024**	0.060	0.463
Calcium	-0.051	0.538	0.148	0.070	-0.037	0.649
Phosphorus	-0.060	0.469	-0.028	0.732	-0.011	0.893
Alkaline phosphatase	-0.007	0.930	0.034	0.677	0.061	0.460
HAM-D			**0.496****	**<0.001**	**-0.421****	**<0.001**
HAM-A	**.496****	**<0.001**			**-0.697****	**<0.001**
MQoL	**-.421****	**<0.001**	**-0.697****	**<0.001**		

CBC: Complete blood count: RBCs: Red blood cells; HCT: hematocrit; MCV: mean cell volume: MCH: mean cell hemoglobin; MCHC: mean cell hemoglobin concentration; WBCs: White blood cells; HA: hemoglobin Alpha; HF: Fetal hemoglobin; * indicate significant differences

DISCUSSION

Thalassemia is one of the commonest causes morbidity and mortality in both developed and developing countries. In the developing countries, thalassemia associated deaths are due to non-compliance of treatment attributed to psychosocial and economic factors. Methods to reduce the burden of thalassemia and its associated comorbidity and mortality include screening, health education, prenatal diagnosis and genetic counselling [14,15].

The current work aimed to explore the psychiatric burden of thalassemia. Results indicated that, the depression and anxiety were significantly increased, while quality of life was significantly reduced in patients with thalassemia than their age and sex matched control peers. The depression and anxiety significantly correlated with quality of life. These changes were attributed to the burden to long-life transfusion dependency and chelation

therapy with frequent hospital admissions, with impaired quality of life [16].

Jaafari *et al*. conducted a meta-analysis to estimate the prevalence of depression among Iranians with thalassemia. They reported that, the pooled prevalence of depression was 42%, while the mild, moderate, severe, and extremely severe depression was 16%, 13%, 13%, and 3%, respectively. The prevalence rate in this meta-analysis is higher than the current study and this could be explained by the fact that, they included all age groups, including adults, where different coping strategies and treatment for depression were practiced. Younger adults or adolescents have low ability to cope with depression and usually need an aid for relatives or care-givers. The study recommended urgent establishment of therapies to reduce depression among Iranian patients with thalassemia [17].

Other probable factors explaining the differences in depression rate in thalassemia include cultural and ethnic differences, and treatment services. The role of culture in the depression and psychological disorders has been well-considered previously [18-20].

The overall depression is higher in thalassemia than control group and this may be attributed to the fact that, thalassemia is a chronic disabling disease, and the feeling of being different may predispose to the development of depression. Physical characters as stunting and lower weight may reduce the self-esteem of patients with thalassemia, which is associated or followed by depression [21]. Besides, another study suggested a genetic susceptibility [22]. Depression in thalassemia reflected on all aspects of life. It may lead to reduction of academic achievement, social isolation, lack of independence and reduced physical activity. All of these impair the patient's quality of life [23].

The current work showed an associated reduction of quality of life in thalassemia than control group. Ismail *et al*. noted that, thalassemia has a negative impact on perceived all quality of life domains (e.g., physical, emotional, social and school achievement) than the healthy children [24]. Similarly, Khodashenas *et al*. [25] and Shafie *et al*. [6] reported that, all domains of quality of life are affected in transfusion-dependent Iranian and Malaysian patients.

Zolaly *et al*. concluded that, patients with thalassemia are at higher risk for developing psychological problems, and this might affect the course of the disease and had short and long-term complications. They advocated early diagnosis and proper support to help patients coping with their disease impact and consequently improve their quality of life [9].

Mild depression and anxiety were the highest among the study populations. Sarhan *et al*. demonstrated that, 78.5% of the Palestinian patients with thalassemia had depression. They attributed this to political conditions, unemployment, inadequate participation in education programs and inability to marry [26].

Behdani *et al*. reported a rate of 26.7%, which was significantly higher than in the control group [27]. Shaligram *et al*. reported depressive symptoms in 62% of thalassemia patients [28]. Cakaloz *et al*. also reported significantly higher rate of depression in children with thalassemia (55.0%) than the control group (14.7%). Anxiety also significantly increased in thalassemia than healthy children (30.0% vs 15.0%) [29].

The heterogeneity in prevalence rates of anxiety and depression in thalassemia in different study could be explained by different scales used for diagnosis, the heterogeneity of patients, their culture and social backgrounds, their coping strategies and supporting services provided. However, results of the current work are in accordance with Behdani *et al*. who reported significant increase of depression, anxiety and significant reduction of the quality of life in children with thalassemia than healthy controls [27].

In conclusion, we reported significant increase of depression and anxiety in adolescent with transfusion-dependent thalassemias. This was associated with significant reduction of patient's quality of life. Psychological assessment and interventional programs are recommended in addition to physiological treatment plan. We expected significant compliance with treatment and improvement of overall outcome with introduction of such programs. Thus, future studies are warranted to introduce and assess such programs.

Future directions: The early detection and diagnosis of depressive symptoms could reduce its intensity, duration and frequency before advancement to severe grades. This could be considered in the future planning of treatment

interventions. A significant part of treatment plane should be directed toward reduction of psychiatric disorders associated with thalassemia. This was suggested by Munoz *et al*. for future treatment planes [30]

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