O R I G I N A L   A R T I C L E

Quality of life among adolescents aged 14 to 18 years with beta-thalassemia major (TM) in Qatar

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Summary. *Background:* Thalassemia is a heterogeneous group of inherited disorders of hemoglobin synthesis. It is a common disease in Mediterranean, Southeast Asia, Indian subcontinent, and Middle East countries, including Qatar. *Purpose:* The aim of this study was to assess the quality of life (QOL) among patients aged 14 to 18 years with thalassemia major (TM) in Qatar and correlates their QOL with bio-demographic data of the patients compared to healthy controls. *Materials and Methods:* This cross-sectional study measured the QOL in adolescents with thalassemia major who were attending ambulatory units in a tertiary hospital in Qatar. Forty children and adolescents with TM and 40 healthy participants were enrolled in the study. Forty-two (52.5%) participants were males and 38 (47.5%) females. Data were collected utilizing PedsQL™ 4.0 generic core scale and were analyzed using the appropriate statistical method. *Results:* Children with TM had significantly lower and more variable overall quality of life score (69.1±16.8) compared to healthy matched children (77±12.8), (p<0.001). Both groups were not different from the physical, emotional, and social domains. Thalassemic adolescents had also a significantly lower school performance. *Conclusions:* TM adversely affects the QOL of children and adolescents and this necessitates applying more efforts to help them improve and achieve a desirable quality of life. Patients with TM need more attention in schools that can be accomplished by implementing a special program for their management that needs a mutual collaboration between Ministry of Public Health (MoPH) and Ministry of Education (MoE) in Qatar. (www.actabiomedica.it)

Key words: quality of life, teenagers, β-thalassemia major, PedsQL™, Qatar

Introduction

Thalassemia is a heterogeneous group of inherited disorders of hemoglobin synthesis. The severe form of the disease (Thalassemia Major, TM) is characterized by severe anemia requiring repeated blood transfusions, iron overload and disease related complications (1-3).

The quality of life (QOL) and survival of children suffering from TM are considerably lower as compared to their normal counterparts (4-6).

One study described that 80% of patients with patients with TM have at least one psychiatric disorder. The most frequent disorders described in thalassemic patients were disembodiment, anxiety, depres-

sion, somatoform disorders and anger. These disorders may also have a negative impact on the social activities and education outcome of these patients (7-14).

In Qatar, there were no data about the QOL in patients with TM. Therefore, this study assessed the QOL of patients with TM in relation to their physical, emotional, social life and school performance in comparison to healthy control group.

Patients and Methods

The purpose of our study

The purpose of this study was to assess the QOL among patients aged 14 to 18 years with TM living in Qatar by utilizing PedsQL™ 4.0 generic core scale and to correlate this measurement model, with their bio-demographic data.

Patients

Patients with TM were recruited out of those attending hematology clinics and Day Care Unit for routine assessment, follow-up, and management in the National Center for Cancer Care & Research (NC-CCR), a member of Hamad Medical Corporation (HMC) in Qatar.

Patients were on regular blood transfusion and iron chelation since early life.

Instrument

The PedsQL™ Measurement Model is a modular approach to measuring health-related quality of life (QOL) in adolescents and those with acute and chronic health conditions. The PedsQL™ Measurement Model integrates seamlessly both generic core scales and disease-specific modules into one measurement system (15). The 23-item PedsQL™ Generic Core Scales were designed to measure the core dimensions of health as delineated by the World Health Organization, as well as role (school) functioning. The 4 Multidimensional Scales and 3 Summary Scores are:

The 4 multidimensional scales are:
- Physical Functioning (8 items)
- Emotional Functioning (5 items)

- Social Functioning (5 items)
- School functioning (5 items)

To calculate the total PedsQL™ score, the mean is computed as the sum of all elements over the number of items answered on all scales. Each item of this tool is rated on a 5-point Likert scale from 0 (Never) to 4 (Almost always) and on a 3-point scale for young children (5-7 years): 0 (Not at all), 2 (Sometimes) and 4 (A lot). The scores for each dimension are calculated as follows: the mean score is represented by the sum of the items over the number of items answered; missing values are replaced by the average score of the remaining items; if more than 50% of the elements in a given scale are missing, the scale scores are not computed. Raw scores are transformed into standardized scores on a scale from 0 to 100 with higher scores representing higher functioning levels.

Reliability

The Cronbach's alpha test of internal consistency was used to assess the reliability of the PedsQL™ questionnaire. The 23-item long survey was found internally consistent, and the Cronbach's alpha (r=0.88) suggested that children understood the Arabicized questionnaire equally reliably. The sub-concepts were also internally consistent, denoting their reliability, Cronbach's alphas were as follows for the four main sub concepts (PF=0.79, EF=0.78, SF=0.71, and SCF=0.81). Few children had missing information on school functioning that decreased the testable sample (N=80) (Table 1).

Sampling technique

Forty children and adolescents with thalassemia major and 40 healthy participants were enrolled in the

Table 1. Cronbach's alpha test of internal consistency and scale reliability (N=80)

Domain	N# items	Cronbach's alpha
Pediatric Quality of Life	23	0.88
Physical Functioning. (PF)	8	0.79
Emotional Functioning (EF)	5	0.78
Social Functioning (SF)	5	0.71
School Functioning (SCF)	5	0.81

study. The estimated sample was calculated using power analysis with the total population of approximately 60 patients with TM followed at NCCCR. Forty-two (52.5%) participants were males and 38 (47.5%) females.

The inclusion criteria for the studied cases were 13-18 years, with a confirmed diagnosis of TM, on regular follow-up and treatment at NCCCR. Written informed consent of the parents/guardians and assent of the children/adolescents was obtained. Patients with other diagnoses or patients who refused to participate in the study, and those with other systemic disorders were excluded from this study.

Data were collected via self-administrative questionnaire. The age-appropriate questionnaires were given to the patients and controls. The responses to the questionnaire were scored quantitatively based on their in accordance with the guidelines of Scoring Pediatric Life Inventory.

The study protocol was approved by Institutional ethical committee of HMC, Doha,Qatar. All procedures were carried out with the adequate understanding and consent of patients (MRC PR. 16272/16).

SPSS version 21 was used in this study. Pearson's correlation test was used to study correlations between variables. The summative analysis was used to compute the means and standard deviations of each of the 23-indicators that comprised the PedQL questionnaire. Relative Importance Index (RII) was used to help understand the differences between the two groups (healthy versus subjects with thalassemia) functionalities and qualities of daily life functions. $p < 0.05$ was considered significant.

Results

Demographics

Eighty children and adolescents were included in the survey, 40 with TM and 40 age and sex matched healthy children (Table 2). Their overall mean age was equal to 16±1.5 years. The majority of them were attending regularly schools (90%) and a few (10%) were out of school. Their family monthly income ranged between (15,00 to 10,000 QAR) and the majority

Table 2. Demographic characteristics of 80 children and adolescents

	Number (SD)	Percentage
Age (years) mean (S.D)	16 (1.5)	100
Sex		
Male	42	52.5
Female	38	47.5
Nationality		
Qatari	15	18.8
Other Nationalities	65	81.3
Educational Level		
Student	72	90
Non-Student	8	10
Family Income		
1500-5000 QAR	16	20.1
5001-10000 QAR	43	53.8
>10000 QAR	21	26.3
Disease Status		
Non-Thalassemia	40	50
Thalassemia	40	50

belonged to families with income of between (5,000 to10,000 QAR), the remainder (26.3%) belonged to families with incomes (>10,000 QAR).

90% of patients with TM were diagnosed between 6 months and 12 months of age. None of the 40 children with TM had hepatitis C infection. 7.5% of them were splenectomized during their course of the disease. 12.5% had other known co-morbidities according to their medical records. The chelation therapy received by those who were undergoing such therapy were either oral Deferasirox treatment (77.5%) or combined oral Deferasirox and subcutaneous Desferal (22.5%) (Table 3).

The summative analysis was used to compute the means, and standard deviations of each of the 23-indicators that comprised the PedQL™ questionnaire, the means, and standard deviations are displayed in table 4 (relative importance index).

To help us to understand the differences between the two children groups (healthy versus thalassemia) functionalities and qualities of daily life functions as measured with the PedsQL™ questionnaire, the Relative Importance Index (RII) was used as an estimate of how relevant (out of a 100%) is the individual functionality to each children groups was when compared

Table 3. Medical and comorbidity characteristics in the children and adolescents with thalassemia major (N=40)

	Frequency	Percentage
Family history of thalassemia		
Yes	36	90
No	4	10
Thalassemia onset		
<6 -12 months	36	90
>12 months	4	10
Frequency of blood transfusions		
every 3 weeks	31	77.5
every 4 weeks	9	22.5
Hepatitis C infection		
Clear	40	100
Positive	0	0
History of splenectomy		
Yes	3	7.5
No	37	92.5
Other comorbidity		
Yes	5	12.5
No	35	87.5
Iron chelation Therapy		
Yes	34	85
No	6	15
Drugs used for the chelation therapy		
Deferasirox	31	77.5
Combined (Deferasirox and Deferoxamine)	9	22.5

Table 4. Descriptive statistics for 80 children's physical and emotional functioning indicators

	Mean (SD)
Physical functioning (PF)	
It is hard for me to have a shower by myself	96.3 (10.6)
It is hard for me to do sports & activities	82.8 (25)
It is hard for me to do chores around the home	80.9 (24.6)
It is hard for me to run	78.5 (25.5)
It is hard for to walk >100 M	77.5 (30.2)
I have aches and pains	72.8 (23.6)
It is hard for me to lift heavy objects	70.3 (26.1)
I feel tired	66.3 (29.8)
Emotional functioning (EF)	
I feel scared or afraid	78.1 (22.6)
I have trouble sleeping	72.2 (31.8)
I feel sad	69.4 (26.7)
I worry what will happen to me	65.6 (33.4)
I feel angry	64.7 (26)
Social functioning (SF)	
Other teenagers tease me	87.3 (21.3)
It is hard to keep up with other teenagers my age	84.7 (19.7)
I have trouble getting along other teenagers	82.8 (27.4)
Other teenagers do not want to be my friend	82.5 (25.9)
I cannot do things other simile teenagers can do	72.5 (30.5)
School functioning, (SCF), n=72	
It is hard to pay attention in the class	68.6 (35.5)
I have trouble keeping up with my school	59 (32)
I forget things	54.2 (29.3)
I miss school because of medical appointments	50.2 (35.2)
I miss school because of not feeling well	50 (34.3)

to each other, this will help us identify the gaps and similarities between the two groups in simpler contexts.

The estimated results of relative importance (RII) score lies between 0 and 1 and can be respresented as a percentage, with higher score represent more relative importance (functionality), and smaller score indicates smaller magnitudes of importance to the respective group. The estimates RII scores for each item comprising the PedsQL™ 23-items are displayed in table 5.

The majority of the restrictions to functionality among thalassemia children appear to be more across functionality within school and attendance to school, mental powers and attentiveness and their restricted ability to do extraneous activities compared to healthy children. Their potent functionality aspects were exemplified into self-caring, acceptance by, friendliness

to and getting along others plus their ability to sustain relations with their peers and similes on age.

According to the RII analysis, it is evident that a pattern of differences is unearthed between the relative functionality of each of the health and the thalassemia groups. The top seven functionalities for the thalassemia group indicated that they were more capable of showering themselves than healthy children, followed by being more teased by others compared to their healthy peers, as well as more inclined to be accepted by others than their healthy counterparts, besides being slightly more capable of keeping up with others and slightly greater ability to do chores of home.

Nonetheless, there appears many similarities as the RII of the other items continues to decrease for the thalassemia when compared to the healthy group, denoting they can be equivalently functional on these items.

Table 5. Comparative Relative Importance Index (RII) score

item#	Item code	Indicator	Subjects with thalassemia RII	Healthy controls RII
5	PFREC5	It is hard for me to have a shower by myself	0.98	0.95
16	SFREC3	Other teenagers tease me	0.93	0.79
15	SFREC2	Other teenagers do not want to be my friend	0.86	0.79
18	SFREC5	It is hard to keep up with other teenagers my age	0.86	0.84
6	PFREC6	It is hard for me to do chores around the home	0.84	0.78
14	SFREC1	I have trouble getting along other teenagers	0.84	0.82
3	PFREC3	It is hard for me to do sports & activities	0.79	0.87
9	EFREC1	I feel scared or afraid	0.79	0.78
7	PFREC7	I have aches and pains	0.76	0.69
2	PFREC2	It is hard for me to run	0.70	0.85
12	EFREC4	I have trouble sleeping	0.70	0.74
10	EFREC2	I feel sad	0.69	0.70
1	PFREC1	It is hard for to walk >100 M	0.67	0.88
4	PFREC4	It is hard for me to lift heavy objects	0.66	0.74
8	PFREC8	I feel tired	0.64	0.68
11	EFREC3	I feel angry	0.64	0.66
17	SFREC4	I can not do things other simile teenagers can do	0.64	0.81
13	EFREC5	I worry what will happen to me	0.58	0.73
19	SCREC1	It is hard to pay attention in the class	0.57	0.77
21	SCREC3	I have trouble keeping up with my school	0.48	0.68
20	SCREC2	I forget things	0.45	0.61
22	SCREC4	I miss school because of not feeling well	0.23	0.72
23	SCREC5	I miss school because of medical appointments	0.20	0.75

However, the bottom ranked functionalities for the thalassemia children unveiled another important difference. As can be seen at the last items at the bottom of table, adolescents with thalassemia missed schools more than healthy controls due to medical appointments or not feeling well, as well as they appear to have had, for having on average more forgetfulness than the healthy adolescents. Also their school functionality and keeping up with school was remarkably less than the controls. Furthermore, their power of attention was relatively lower than their healthy peers as well. In addition, they reported to have had more worries about their future when compared to the healthy average subjects and were unable to do things equally to their counterparts.

Subjects with thalassemia reported, substantially, a lower functionality (ability) to walk more than 100 meters and to do running than the healthy controls, according to their reported Relative functionality.

The compute function in the SPSS analytical program was used to calculate the overall means of the domains that comprise the PedsQL™ as described by (author, year). The overall means for these concepts (i.e., perceptions) were computed and divided by the total number of each main concepts, after coding and transforming them into a metric score between 0-100, with 100 denoting greater functionalities, not weakness.

The overall mean pediatric QOL score for patients with TM was equal to 73 points, the overall mean physical functioning for all the subjects was equivalent to 78.2 points denoting that these adolescents were capable of functioning physically, regardless of their disease and health status. The overall social functioning of these adolescents was slightly higher than the rest of the other functionalities (82 points). Finally, the school functioning was low for all subjects with TM, with overall mean equivalent equal to 56.8 points (Table 6).

The Pearson's r was used as a measure of association between the overall Pediatric QOL score, and

Table 6. PedsQL™ Scoring

Items	Mean (S.D)
Overall Pediatric Quality of Life Score	73 (15)
Physical Functioning (PF)	78.2 (16)
Emotional Functioning (EF)	70 (20.7)
Social Functioning (SF)	82 (17.2)
School Functioning (SCF)	56.8 (24.9)

it's sub-domain concepts (Table 7). Greater Pediatric QOL was significantly associated with better physical performance of adolescents (r=0.87, p<0.01). In addition, QOL was significantly associated with social functioning (r= 0.73, p<0.01) and school performance was significantly associated with better QOL (r=0.66, p<0.01) Older subjects tended to report significantly worse QOL (r=-0.3, p<0.05), significantly poorer physical functionality (r=-0.32, p<0.005) and emotional functioning (r=-0.30, p<0.05). On the other hand, a better academic performance was associated with greater physical functioning (r=0.36, p<0.01) and better emotional functioning (r=0.26, p<0.05). Social functioning among adolescents was significantly associated with their physical functioning (r=0.65, p<0.01) and emotional functioning (r=0.54, p<0.01) (Table 7).

The comparison on the main demographic and quality of life perceptions between adolescents with thalassemia and healthy controls is displayed in table 8.

Subjects with TM had significantly lower school attendance versus the healthy controls (chi-squared test, χ^2(1)=6.9, p=0.009). It was evident that more adolescents with thalassemia (32.5%) belong to families with smaller incomes (1500-5000 QAR) compared to healthy controls (7.5%).

Adolescents with BTM had significantly lower and more variably overall QOL score (69.1±16.8) compared to healthy children (77.5± 2.8), (p<0.001). Thalassemic patients had lower school functioning (38.8±22.7) versus healthy controls (71.2±15.2). (p<0.001) There was no statistical difference between the two groups regarding physical, emotional or social functioning.

Discussion

The results of this study showed that adolescents with TM had lower overall QOL compared to their healthy peers. They had markedly decreased academic performance. In this study, 10% (N=8) of the patients left the school at certain point of their life; all of them were not Qataris. Several studies in the region reported greater educational challenges among patients with thalassemia compared to their healthy peers (16-18). Patients with thalassemia often forced to miss school because of hospital appointments or admissions for regular monthly blood transfusion and/or treatment of complications (19).

Our study showed that the mean of dimensions of QOL was significantly lower in the patient's group compared with the control group. These results were consistent with those obtained by Ismail et al. in Malaysia (20), Cheuk et al. in Hong Kong (21), Baraz et al. in Ahvaz-Iran (17), Clarke et al. in UK (22), Thavorncharoensap et al. in Thailand (23), Surapolchai et al. in Thailand (24), Salama et al. in UAE (25), Garaibeh et al. in Jordan (26), Caocci et al. in Italy (19), Khaledi et al. in Iran (27), Ansari et al. in Iran (28), Sultana et al. in Pakistan (29), Grewal et al. and Sharma et al. in India (30, 31), Tuysuz et al. in Turkey (32).

Table 7. Correlations between children's perceptions of physical, emotional, social and school functioning with the total Pediatric Quality of Life and age

	PedsQL™	PF	EF	SF	SCF	N
Physical Functioning (PF)	.866**					80
Emotional Functioning (EF)	.818**	.709**				80
Social Functioning (SF)	.734**	.552**	.543**			80
School Functioning (SCF)	.654**	.357**	.261*	.262*		72
Age (years)	-.287**	-.318**	-.254*	-.103	-.196	80

**Correlation is significant at the 0.01 level (2-tailed).* Correlation is significant at the 0.05 level (2-tailed)

Table 8. Difference between adolescents with thalassemia and healthy controls in relation to demographic keys and QOL perceptions

	Healthy controls (n=40) Mean (SD)	Thalassemia patients (n=40) Mean (SD)	Test statistic	P value
Age (years)	15.8 (1.5)	16.3 (1.5)	U(80)=1.49	0.136
Sex				
Male	20 (50%)	22 (55%)	χ^2 (1)=0.201	0.654
Female	20 (50%)	18 (45%)		
Nationality				
Qatari	6 (15%)	9 (31%)	χ^2 (1)=0.738	0.390
Other Nationalities	34 (85%)	31 (77.5%)		
Educational Level				
Student	40 (100%)	32 (80%)		0.009
Non-Student	0	8 (20%)		
Family Income				
1500-5000 QAR	3 (7.5%)	13 (32.5%)	χ^2 (2)=18.5	<0.001
5001-10000 QAR	31 (77.5%)	12 (30%)		
>10000 QAR	6 (15%)	15 (37.5%)		
Family history of TM				
Yes	0	36 (90%)	χ^2 (1)=65.5	<0.001
No	40 (100%)	4 (10%)		
Pediatric QOL	77 (12.8)	69.1 (16.2)	U(80)=2.5	0.013
Physical Functioning (PF)	80.8 (13.9)	75.5 (17.6)	U(80)=1.4	0.163
Emotional Functioning (EF)	72.1 (17.1)	67.9 (23.9)	U(80)=1.3	0.187
Social Functioning (SF)	81.5 (19.8)	82.5 (14.4)	U(80)=0.02	0.988
School Functioning (SCF)	71.2 (15.4)	38.8 (22.7)	U(80)=5.5	<0.001

Garaibeh et al. (26) compared the outcomes of PedsQL™ obtained on a sample of 128 Jordanian children with thalassemia (aged 8-18y) with 83 healthy controls. Although their patients had significantly lower HRQOL, mean scores in all dimensions, supporting of our findings, the lowest mean score was reported for the school domain (46.7).

Several recent studies have used PedsQOL™ 4.0 to assess the quality of life in thalassemia patients (20-32). Sultana et al. (29) reported the data obtained in 266 Pakistani patients (2-18 years; mean age at diagnosis:10.43±12.0 months). The results showed a 5% to 10% reduction in psychosocial and emotional functioning in patients with no significant association with age, gender and number of blood transfusions.

Grewal et al. (30) conducted a qualitative, comparative, cross-sectional study in a tertiary hospital in India to evaluate QOL of 35 TM adolescents (10-18 years) compared with 35 healthy participants. More

than half of the adolescents with thalassemia had poor QOL. There was no statistically significant association between QOL and socioeconomic status in both groups. The authors proposed that provision of subsidized organized care did not impact on poor socioeconomic status on QOL of patients with thalassemia.

Sharma et al. (31) evaluated PedsQL™ scores in 75 Indian patients with thalassemia and 80 healthy participants. Total QOL score was significantly lower in cases as compared with controls even after adjusting for demographics. It was found that caregivers of children with TM were more likely reporting poor health in their children compared with parents for controls (odds ratio: 15.8, 95% confidence intervals: 2.8-89.9).

Tuysuz et al. (32) compared the outcomes of PedsQL™ obtained on a sample of 80 Turkish children and adolescents with thalassemia (aged 5-18 years) compared to 80 age and sex-matched healthy controls. They stated that transfusion-dependents patients and

Table 9. Studies addressing QoL among thalassemia patients

Authors and Reference	Year - Place	Number	Age (yrs)	Findings
Ismail et al. (20)	2006 - Malaysia	78	5-18	Of the 96 thalassaemic patients approached, 78 gave consent to be interviewed giving a response rate of 81.3%. Out of 235 healthy controls approached, all agreed to participate giving a response rate of 100%. The mean age for the patients and schoolchildren was 11.9 and 13.2 years, respectively. After controlling for age and demographic background, the thalassemia patients reported having significantly lower QOL than the healthy controls.
Cheuk et al. (21)	2008 - Hong Kong	98	5-18	PedsQL revealed post-transplant patients rated better for running (3.53 vs 2.72, P=0.001) and sports (3.20 vs 2.64, P=0.038), even after adjustment for comorbidities, but were less satisfied for school absence (2.53 vs 3.29, P=0.03). In conclusion, transplanted thalassemic patients enjoy better QOL, mainly in physical health, compared with conventionally treated patients.
Clarke et al. (22)	2010 - UK	22	8-18	Child behaviour was within the normal range but child HRQOL was significantly lower than population norms. Family financial concerns associated with TM were associated with poorer child HRQOL (P=0.020).
Thavorncharoensap et al. (23)	2010 - Thailand	315	5-18	The academic performance subscale scored the lowest, with a mean of 67.89 (SD=15.92). The following factors significantly affected the QOL of the patients: age; age at onset of anemia and age at first transfusion; pre-transfusion hemoglobin (Hb) level; receiving a blood transfusion during the previous three months; and disease severity. In addition, iron chelation therapy had a significant negative effect on QOL in the school functioning subscale.
Surapolchai et al. (24)	2010 - Thailand	75	2-18	The stepwise multiple regression analysis indicated that total QOL score of child self-report was negatively predicted by lower family income, early age onset of anemia before 2 years. The negative predictors of total QOL score of parent proxy-report were regular transfusion every 1-2 months, while self-medical payment was positively predictive.
Salama et al. (25)	2011 - UAE	279	≥13	Overall QOL mean score (±SD) was 78.88 (±13.14). Out of 5 predictors affecting the total score (type of diagnosis, annual serum ferritin, number of complications, diabetes mellitus and (hypogonadism) sexual growth complications) it was found that the total summary score was positively predicted by diagnosis (p=0.018).
Garaibeh et al. (26)	2012 - Jordan	128	8-18	Thalassaemic children had significantly lower QOL mean scores in all dimensions compared with their healthy counterparts. The lowest mean scores for thalassaemic children were reported for the school functioning and the physical functioning domains, respectively. Regression analysis showed that disease complications and family history of thalassaemia explained 8.5% of the variance in the total QOL.

(continued)

Table 9 *(continued)*. Studies addressing QoL among thalassemia patients

Authors and Reference	Year - Place	Number	Age (yrs)	Findings
Caocci et al. (19)	2012 - Italy	60	5-17	The scores of parents were generally lower than those of their children for Emotional Functioning (mean 75 vs 85; p=0.002), Psychosocial Health Summary (mean 70.3 vs 79.1; p=0.015) and the Total Summary Score (mean 74.3 vs 77.7 p=0.047). QOL was not associated with ferritin levels, hepatomegaly or frequency of transfusions or iron chelation therapy. Multivariate analysis showed that a delayed start of iron chelation had a negative impact on total Peds QOL scores of both children (p=0.046) and their parents (p=0.007).
Khaledi et al. (27)	2013 - Iran	80 (half of them are healthy control)	≥18	Results related to the quality of life showed that QOL was lower than control group (P<0.05).
Ansari et al. (28)	2014 - Iran	301 (51 participants as controls)	≥18	QOL was lower in patients compared to the controls (P<0.05). Age, higher education level, lower ferritin level and using oral iron chelator were associated with better QOL scores. On the other hand, cardiac disease, hepatitis C and history of psychiatric disorders were associated with impaired QOL scores.
Sultana et al. (29)	2016 - Pakistan	266	2-18	Psychosocial health summary score was 75.37±25.79 versus 70.73±23.16 with p value of 0.04. Mean score for emotional functioning was 75.38±28.89 versus 67.31±23.51 (p=0.00). No significant association with age, gender and number of blood transfusion was found on perception of health related QOL.
Grewal et al. (30)	2017 - India	70 (half of them are healthy control)	10-18	Almost half of the thalassemic adolescents had poor QOL. There was no statistically significant association between QOL and socioeconomic status in both groups. The social domain was the major contributor to poor QOL in thalassemics.
Sharma et al. (31)	2017 - India	75 thalassemic and 80 non-thalassemic children	2-18	The total QOL score was significantly lower in cases as compared with controls. Even after adjusting for age, sex, socio-economic status, and total QOL score by the parent, it was found that caregivers of thalassemic children were significantly more likely to report poor health compared with those of controls.
Tuysuz et al. (32)	2017 - Turkey	80 pediatric TDT patients	5-18	Transfusion dependen thalassemia patients and their parents rated lower QOL scores in all domains (physical, emotional, social, and school functioning) compared with the healthy population (P<0.01). The univariate analysis indicated that the total QOL score for children's self-reports was negatively predicted by high ferritin levels and the presence of any complication. The only negative predictor of the total QOL score in multivariate analyses was a high ferritin level (>1800 ng/ml).

their parents rated lower HRQOL scores in all Ped-sQL™ domains compared with the healthy population (P<0.01) especially those with high serum ferritin levels (>1800 ng/mL).

Our study, as with a majority of the previous studies highlighted the importance of implementing a unique perspective of health-related QOL by evaluating both child-self and parent-proxy reports.

Conclusions

The results of the current study indicated a significant reduction in school functioning in children with thalassemia compared to healthy participates. Improving the collaboration between Ministry of Public Health (MoPH) (Medical staff and hospital staff) and Ministry of Education (MoE) (teachers, counselors, and social workers) appears necessary for these patients to achieve better QOL and school performance.

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