Health-related Quality of Life in Children and Adolescents With β-Thalassemia Major on Different Iron Chelators in Basra, Iraq

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Summary: Few studies have investigated the quality of life of children with thalassemia in the Middle East or Mediterranean region, especially Iraq. Therefore, this study was performed to assess the health-related quality of life (HRQoL) of patients with β-thalassemia major compared with healthy children and adolescents in the same age group and to evaluate the effects of different iron chelators on HRQoL measurements. A case-control study was performed on patients with β-thalassemia major registered at the Center for Hereditary Blood Diseases in Basra from February 2012 through July 2013. The group included children and adolescents aged 2 to 17 years old. HRQoL was assessed using the Pediatric Quality of Life (PedsQL) Generic Core Scale questionnaire, version 4.0, for children 2 to 12 years old and the Short Form-36 health survey questionnaire, version 2 (SF-36v2), for children and adolescents aged 13 to 17 years old. A total of 209 age-matched and sex-matched children and adolescents were included in the control group. The study did not find a significant difference in PedsQL scores among different age groups or different iron chelators, whereas there were significant differences in all of the SF-36v2 domains, with the best quality of life observed in the deferasirox group, followed by the deferoxamine group and the combined therapy group ($P < 0.05$). The use of deferasirox among patients aged 13 to 17 years old was associated with higher SF-36v2 scores than in the other groups ($P < 0.05$). However, for younger patients, the PedsQL scores were not significantly different for different iron chelators. The use of oral deferasirox significantly improved the quality of life of adolescents with β-thalassemia major. However, this effect was less prominent among patients aged 2 to 12 years old.

Key Words: quality of life, iron chelators, β-thalassemia major

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Thalassemia is becoming a serious public health problem throughout the Mediterranean region, Middle East, Indian subcontinent, and Southeast Asia.[1] Approximately 3% of the world's population carry genes for β-thalassemia (β-TM).[2] β-TM is encountered at different frequencies in almost all Arab countries with carrier rates of 1% to 11%, and the frequency is high in Lebanon, Jordan, Iraq, Palestine, Egypt, and other Arab countries.[3] In Iraq, the carrier rate of β-TM in different governorates ranges between 3.7% and 6.5%.[4] In Basra, the frequency of β-TM traits ranges from 3.3% to 7.9%, with an overall frequency of 4.6%.[5]

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β-TM has significant effects on physical health, which can lead to physical deformity, growth retardation, and delayed puberty. Its effect on physical appearance, for example, bone deformities and short stature, contributes to poor self-image.[6,7] Severe complications, such as heart failure, cardiac arrhythmia, liver disease, endocrine complications, and infections, are common among thalassemia patients; these problems do not only affect patients' physical functioning but also their emotional functioning, social functioning, and school performance, leading to impaired health-related quality of life (HRQoL) in these patients.[6,7] The effect of the disease on many aspects of life becomes increasingly evident during the preschool and school ages, when children seek independence and become more aware of the differences between themselves and others, which are attributed to either the physical dimension (facial appearance, stunted growth, or bone deformities) or their inability to perform daily tasks and physical activities.[8]

Cumulative iron burden is an inevitable consequence of ongoing transfusion therapy. In β-TM patients, increased gastrointestinal tract iron absorption can result from severe anemia and ineffective erythropoiesis.[9]

Three iron chelators are available: deferoxamine (DFO), which requires intravenous or subcutaneous parenteral administration; and 2 other oral iron chelators, deferiprone (DFP) and deferasirox (DFX). DFX is an orally ingested, highly bioavailable chelator that is absorbed in the GI tract.[10] Improvements in iron chelation therapy (ICT) administration, convenience, and tolerability are expected to improve patients' satisfaction with ICT and their HRQoL.[11] Only DFO and DFX are available in Iraq for the treatment of iron overload (IOL).

Because β-TM is a chronic disease that requires lifelong treatment and a cure is not achievable, the assessment of HRQoL is essential for the provision of proper care because it facilitates the identification of the effects of the disease and its treatment from the children's perspective. In addition, there is existing evidence indicating that thalassemia has a negative effect on HRQoL.[6]

Few studies on the quality of life (QoL) of children with thalassemia have been published in the Middle East and Mediterranean region.[12,13] Therefore, this study was undertaken to assess the HRQoL of patients with β-TM compared with healthy children and adolescents of same age group and to evaluate the effects of different iron chelators on HRQoL measurements.

MATERIALS AND METHODS

This study was a case-control study that was conducted in patients with β-TM registered at the Center for Hereditary Blood Diseases in Basra over an 18-month

period from February 2012 through July 2013. The study included children and adolescents aged 2 to 17 years old on iron chelating agents: DFO, DFX, or both.

In addition to age and sex, further information was recorded: educational levels of the child (if of school age) and both parents, age at diagnosis, type of ICT, previous surgical operations performed on the patient, frequency of blood transfusions (BTs), the average number of BTs/year, and associated complications (diabetes mellitus, hepatitis C, and cardiac complications).

The hemoglobin before the last BT and serum ferritin were also recorded. The patients were categorized into 2 groups according to their serum ferritin levels: <2500 and ≥ 2500 ng/mL.[14]

The control group included age-matched and sex-matched, apparently healthy children and adolescents who were free of any chronic conditions, including hemoglobinopathies.

Data were collected from the control group by visiting 4 primary and secondary schools and 2 primary health centers.

Informed consent was obtained from the child and one of his or her parents before recruitment into the study. In addition, the Basra Health Directorate and the Basra Education Directorate approved the study before it began. This work was also approved by the Ethical Committee of Basra Medical College.

HRQoL Questionnaires

HRQoL was assessed using the Pediatric Quality of Life (PedsQL) Generic Core Scale questionnaire, version 4.0, for children 2 to 12 years old, and the Short Form-36 health survey questionnaire, version 2 (SF-36v2), for children and adolescents aged 13 to 17 years old.[12,15]

The PedsQL questionnaire was used to evaluate β-TM patients aged 2 to 12 years old. Separate questionnaire forms for children aged 2 to 4, 5 to 7, and 8 to 12 years old were used. The PedsQL Generic Core Scale, version 4.0, is a 23-item multidimensional model that includes the essential core domains for pediatric HRQoL measurement: Physical Functioning (8 items), Emotional Functioning (5 items), and Social Functioning (5 items), as indicated by the World Health Organization, as well as School Functioning (5 items).

The children's self-reports and parent proxy reports in the PedsQL measurement model are sensitive to cognitive development, and they including appropriate forms for children 5 to 7 and 8 to 12 years old and their parents.[7]

For patients who were 2 to 4 years old, questions concerning Physical, Emotional, Social, and School Functioning were answered by one of their parents.

An Arabic version of PedsQL was administered after completing the PedsQL-core user agreement form. The reliability, validity, responsiveness, and practicality of the PedsQL Generic Core Scales have been assessed in both physically healthy pediatric populations and pediatric populations with acute and chronic health conditions. The internal consistency reliability of the PedsQL 4.0 Generic Core Scale approached 0.90 for self-reporting.[16]

The SF-36v2 is a well-recognized, short-form health survey containing only 36 questions that is used mainly for individuals older than 12 years and that can be self-administered or administered by a trained interviewer. It is a generic instrument that consists of 8 subscales and 2 major (summary) measurements. The 8 subscales include Physical Functioning (PF), Role-Physical (RP), Bodily Pain (BP), General Health (GH), Vitality (VT), Social Functioning (SF), Role-Emotional (RE), and Mental Health (MH). The 2 major (summary) measurements are the Physical Health Component Score (PCS) and Mental Health Component Score (MCS).[17]

This questionnaire was used for children aged 13 to 17 years old because it is self-administered by the participants; many of patients consulted the Center for Hereditary Blood Diseases without an adult caregiver, and the subjects in the control group were interviewed at school.

In addition, it was found that, in children younger than 11 years old, complementary information could be gained from questioning children and parents, whereas for children older than 11 years of age, parents provided little information beyond that obtained by interviewing the child.[18]

Reliability estimates for Physical and Mental Summary Scores usually exceed 0.90. The median reliability coefficients for each of the 8 scales were ≥ 0.80, except for SF, which had a median reliability across studies of 0.76. The validity of this questionnaire is 80% to 90%.[17] The Arabic version of the SF-36 was used. The SF-36 has been translated and adapted in many Arabic countries. An evaluation of the cross-cultural adaptations of this instrument indicated moderate to good quality.[12] The median Cronbach α for the Arabic RAND-36 in multiple subgroups exceeded 0.70 for most of the scales.[19]

The responses to each questionnaire were scored quantitatively based on the answers in accordance with the guidelines for the questionnaires.[17,20] Higher scores indicated better QoL.

Statistical Analysis

Statistical analyses were performed using the Statistical Packages for the Social Sciences (SPSS) software, version 20.0 (Chicago, IL). Comparisons of proportions were performed by cross-tabulation using the χ^2 test.

The t test was used for quantitative comparison and between the means of 2 different samples. Comparisons between groups were performed using 1-way analysis of variance (ANOVA).

Univariate analysis was used to study the correlations between patient characteristics and the PedsQL and SF-36v2 scores. P-values <0.05 were considered statistically significant.

RESULTS

A total of 138 patients with β-TM and 209 healthy children and adolescents were included in this study. Their ages ranged from 2 to 17 years old, with a mean age of 9.36 ± 4.48 for the patients with β-TM and 9.16 ± 4.56 for the control group. The children and adolescents were divided into 4 age groups: 2 to 4, 5 to 7, 8 to 12, and 13 to 17 years old (Table 1). Of 101 patients with β-TM, 22 (21.78%) had left school because of their illness, and 19 (18.81%) had not enrolled in school at all. In addition, the children in the healthy control group and their parents had higher educational levels than the patient group ($P < 0.05$).

The patients were divided into 3 groups based on the type of ICT they were receiving: a DFO group, a DFX group, and a combined therapy group (DFO + DFX). The majority of patients were receiving DFX (60.87%), whereas only 10.87% of patients were receiving combination therapy (Table 2). The DFO group showed a higher

TABLE 1. Distribution of Patients With β-TM and the Control Group According to Age, Sex, and Educational Level

Variables	N (%) Patients (N = 138)	Control Group (N = 209)	*P*
Age (y)			
2-4	27 (19.57)	48 (22.97)	0.873
5-7	25 (18.12)	39 (18.66)	
8-12	44 (31.88)	59 (28.23)	
13-17	42 (30.43)	63 (30.14)	
Sex			
Female			
2-4	15 (19.23)	19 (17.76)	0.213
5-7	11 (14.10)	20 (18.69)	
8-12	30 (38.46)	35 (32.71)	
13-17	22 (28.21)	33 (30.84)	
Total	78 (56.52)	107 (51.20)	
Male			
2-4	12 (20.00)	29 (28.43)	0.238
5-7	14 (23.33)	19 (18.63)	
8-12	14 (23.33)	24 (23.53)	
13-17	20 (33.33)	30 (29.41)	
Total	60 (43.48)	102 (48.80)	
Educational level of children and adolescents			
Illiterate	19 (18.81)	7 (4.73)	0.0001
Primary	64 (63.37)	74 (50)	
Secondary	18 (17.82)	67 (45.27)	
Educational level of mothers			
Illiterate	17 (12.32)	10 (4.78)	0.0001
Primary	56 (40.58)	44 (21.05)	
Secondary	53 (38.41)	70 (33.49)	
Higher education	12 (8.69)	85 (40.67)	
Educational level of fathers			
Illiterate	12 (8.70)	3 (1.44)	0.0001
Primary	43 (31.16)	39 (18.66)	
Secondary	50 (36.23)	60 (28.71)	
Higher education	33 (23.91)	107 (51.20)	

pretransfusion Hb and more frequent transfusion requirements/year than the other 2 groups ($P < 0.05$), whereas the mean serum ferritin level in the DFX group was significantly lower than in the other 2 groups ($P < 0.05$).

The HRQoL dimensions assessed by PedsQL, as reported by the patients, were significantly better among healthy children than among patients with β-TM aged 8 to 12 years old in all dimensions ($P < 0.05$). However, the patients aged 5 to 7 years old reported significantly lower physical, emotional, and total summary scores ($P < 0.05$; Fig. 1).

The parental responses to the PedsQL questionnaires of their children aged 2 to 12 years old were assessed. The total summary score and psychosocial health score were not included in the 2- to 4-year-old age group because there was no School Functioning dimension in this age group (Fig. 2). Parents of healthy children reported significantly higher scores in the emotional dimension only compared with patients with β-TM, as reported by the parents of children aged 2 to 4 years old ($P < 0.05$).

For patients 5 to 7 years old, the physical, emotional, and total summary scores were significantly lower than those of healthy children, whereas among the 8- to 12-year-old age group, parents of patients with β-TM reported lower scores in all dimensions.

The study did not demonstrate significant differences in any dimensions between male and female patients (patients and parent proxies) aged 2 to 12 years old ($P > 0.05$). In addition, no significant differences between child and parent reports were observed in any dimensions ($P > 0.05$; Table 3).

HRQoL assessed by the SF-36v2 was evaluated for all adolescents aged 13 to 17 years old. The mean SF-36 scores of healthy adolescents aged 13 to 17 years old were significantly higher than those of patients with β-TM in the same age group and in all dimensions ($P < 0.001$), with general health being most affected among the patients with β-TM (Fig. 3).

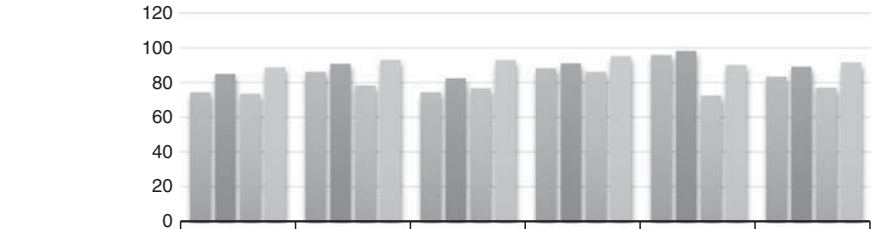
Among patients 13 to 17 years old, there were no statistically significant differences in any dimensions between boys and girls ($P > 0.05$).

All of the children (27) aged 2 to 4 years old were on DFX, and only 4 children aged 5 to 7 years old were on DFO, with the remainder on DFX (21). Regarding the PedsQL scores for children aged 2 to 4 years old, the mean Physical Functioning score was 73.84 ± 8.76, the Emotional Functioning score was 68.15 ± 19.86, and the Social

TABLE 2. Selected Clinical and Laboratory Variables of Patients Receiving ICT

Variables	Total	DFO (N = 39) (28.26%)	DFX (N = 84) (60.87%)	Combined (DFO + DFX) (N = 15) (10.87%)	*P*
Sex (n [%])					
Male	60 (43.48)	20 (51.28)	34 (40.48)	6 (40)	0.510
Female	78 (56.52)	19 (48.72)	50 (59.52)	9 (60)	
Age at disease onset (mo)*	10.92 ± 6.80	12.54 ± 2.69	7.47 ± 4.36	11.26 ± 3.58	< 0.0001
Age at start of ICT (y)*	5.03 ± 2.40	5.78 ± 2.11	4.67 ± 2.44	4.92 ± 2.63	0.053
Pretransfusion Hb (g/dL)*	7.19 ± 0.99	7.52 ± 0.96	7 ± 0.97	7.39 ± 0.82	0.016
Frequency of BTs/y*	16.53 ± 7.24	21.26 ± 10.51	15.36 ± 7.17	16.53 ± 5.57	0.001
Ferritin level at time of the study (ng/mL)*	4733 ± 3244	7798.87 ± 3221.52	3485.11 ± 2420.40	3862 ± 1563.64	< 0.0001
Splenectomy (n [%])	31 (22.46)	15 (38.46)	5 (5.95)	11 (73.33)	0.001
Associated complications (n [%])					
Hepatitis C infection	12 (8.70)	4 (10.25)	4 (4.76)	4 (26.67)	0.020
Cardiac problems	15 (10.87)	8 (20.5)	6 (7.14)	1 (6.67)	0.176
Diabetes mellitus	1 (0.72)	—	—	1 (6.67)	—

*Values are expressed as the mean ± SD; ANOVA was used for these variables.
BT indicates blood transfusion; DFO, deferoxamine; DFX, deferasirox; ICT, iron chelation therapy.



	Physical Functioning	Psychosocial Health Summary Score	Emotional Functioning	Social Functioning	School Functioning	Total Summary Score
Patients (5-7Y)	74.36	86.15	74.3	88.18	95.83	83.33
Control (5-7Y)	84.94	90.76	82.37	91.03	98.15	89.14
Patients (8-12 Y)	73.51	78.33	76.59	86.14	72.5	76.96
Control (8-12 Y)	88.77	92.97	92.88	95.08	90	91.56

FIGURE 1. PedsQL scoring for patients with β-TM and the control group aged 5 to 12 years old. Values are expressed as the mean ± SD. The independent *t* test was used.

Functioning score was 90.56 ± 9.02. For children 5 to 12 years old, there were no significant differences in PedsQL scores (patients' and parents' reports) among the different age groups and different iron chelators (Table 4).

Of the 42 patients aged 13 to 17 years old, 22 were on DFO, 14 were on DFX, and 6 were on combined DFO and DFX therapy. Significant differences in all SF-36v2 domains were reported, with better HRQoL for the DFX group, followed by the DFO group and the combined group ($P < 0.05$).

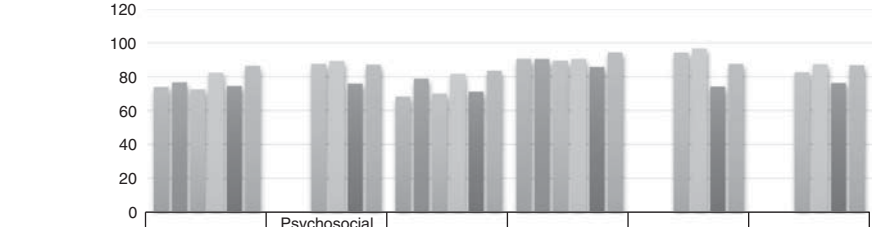
Univariate analysis was used to analyze the correlations between patient characteristics and the PedsQL and SF-362 scores. There were no statistically significant associations between the PedsQL scores and age (except for School Functioning for children 5 to 7 y old), sex, serum ferritin level, and type of iron chelator ($P > 0.05$). However, significant correlations were reported between maternal education level and Psychosocial Functioning and School Functioning and between father's education level and Social Functioning ($P < 0.05$; Table 5).

Among patients aged 13 to 17 years old, significant correlations were found between serum ferritin level and all domains, and patients with serum ferritin levels < 2500 ng/mL had better HRQoL scores than those with higher levels, except for the Mental Health and Mental Component score ($P < 0.05$). The type of iron chelator also had significant effects on all scales; the use of DFX was associated with higher scores than the other groups ($P < 0.05$, Table 6).

DISCUSSION

QoL has become an important tool in the care of patients with β-TM, especially because of the increased survival of patients resulting from better assessment and treatment of IOL, improved adherence to therapy, and younger age at the start of therapy.[21]

Good HRQoL is one of the main goals of the management of β-TM patients because it provides a better understanding of the burden of disease that patients



	Physical Functioning	Psychosocial Health Summary Score	Emotional Functioning	Social Functioning	School Functioning	Total Summary Score
Patients (2-4 Y)	73.84		68.15	90.56		
Control (2-4 Y)	76.66		78.83	90.53		
Patients (5-7 Y)	72.5	87.55	70	89.4	94.17	82.61
Control (5-7 Y)	82.37	89.26	81.67	90.51	96.67	87.4
Patients (8-12 Y)	74.43	75.84	71.14	85.71	74.17	76.27
Control (8-12 Y)	86.39	87.08	83.47	94.28	87.56	86.77

FIGURE 2. PedsQL parents' proxy reports of patients with β-TM and the control group of children aged 2 to 12 years old. Values are expressed as the mean ± SD. The independent *t* test was used.

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TABLE 3. PedsQL Children's and Parents' Reports for Patients 5 to 12 Years Old With β-TM

Dimension	Child Report	Parent Proxy Report	*P*
5-7 y old			
Physical Functioning	74.36 ± 14.89	72.50 ± 12.04	0.629
Emotional Functioning	74.30 ± 18.87	70 ± 18.19	0.416
Social Functioning	88 ± 18.09	89.40 ± 16.03	0.773
School Functioning	95.83 ± 7.93	94.17 ± 8.21	0.618
Psychosocial Health Summary Score	86.15 ± 12.11	87.55 ± 5.75	0.721
Total summary score	83.33 ± 9.56	82.61 ± 4.59	0.647
8-12 y old			
Physical Functioning	73.51 ± 18.34	86.39 ± 7.22	0.812
Emotional Functioning	76.59 ± 19.28	83.47 ± 8.47	0.248
Social Functioning	86.14 ± 15.62	94.28 ± 11.74	0.911
School Functioning	72.5 ± 20.96	87.56 ± 11.23	0.924
Psychosocial Health Summary Score	78.33 ± 15.45	87.08 ± 8.80	0.431
Total summary score	76.96 ± 14.94	86.77 ± 6.62	0.770

Values are expressed as the mean ± SD.
The independent *t* test was used.
β-TM indicates β-thalassemia; PedsQL, Pediatric Quality of Life.

experience, improves patient-provider communication, and can predict morbidity and mortality among these patients.[22]

Therefore, this study was conducted to assess the QoL of patients with β-TM receiving different ICTs and identify the parameters affecting their QoL.

In this study, the children in the healthy control group and their parents had higher educational levels than the patient group; a similar result was reported by Baghianimoghadam et al in Iran[1] and by Ismail and Campbell[23] in Malaysia.

The mean serum ferritin level of the patients with β-TM in this study was comparable with that reported by Ismail et al[16] in Malaysia: 4739.45 ng/mL. However, this level was higher than that of Thai thalassemic patients: 2473 ng/mL.[14] This difference can be explained by the older mean age of the patients when starting ICT among thalassemic patients in Basra.

Patients with β-TM are susceptible to the development of IOL; therefore, ICT is vital for preventing excess iron buildup in the body and the morbidity and mortality that can result.

In this study, approximately 61% of β-TM patients were receiving DFX, whereas only 10.87% of cases were receiving combined therapy (DFO + DFX). This finding was in contrast to those of the study by Torcharus and Pankaew[14] in Thailand, in which only 32.7% were receiving DFX, and in agreement with the study of Goulas et al[24] in Greece, in which more than half of the patients were on DFX, although the included patients were mainly adults aged 18 to 25 years old. This difference could be attributed to the once-daily administration of DFX compared with injectable DFO and the issue of noncompliance with DFO.

Serum ferritin is a measurement for testing IOL in patients with β-TM receiving ICT. This study revealed that the mean serum ferritin level in the DFX group was significantly lower than in the other 2 groups. Ayoub et al[12] did not report a significant difference in serum ferritin among patients on different iron chelators.

To assess HRQoL in β-TM patients, both the PedsQL Generic Core Scale, version 4.0, and the SF-36v2 were used because of their good psychometric standards and cross-cultural adaptability.[23]

This study showed that the scores on all of the PedsQL dimensions for patients aged 8 to 12 years old were significantly lower than those of the control group. This result was similar to that reported by Gharaibeh and Gharaibeh[25] in Jordan, whereas among those aged 5 to 7 years old, only the Physical, Emotional, and Total Summary scores were significantly lower than in the control group. Wahyuni et al[26] in Indonesia and Ismail et al[16] in Malaysia reported lower PedsQL scores among thalassemic patients aged 5 to 18 years old compared with control groups.

Similarly, the parents' perception scores for PedsQL dimensions were in agreement with their children's reports.

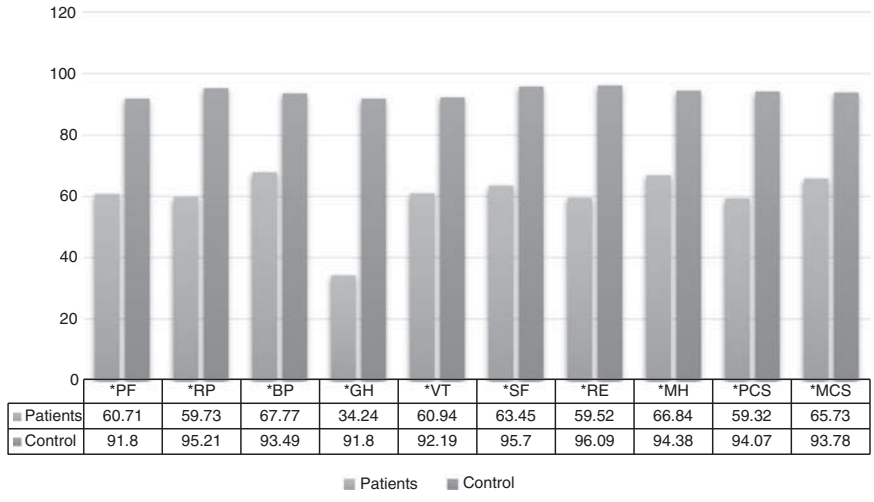

FIGURE 3. SF-36v2 scores of patients with β-TM and the control group. Values are expressed as the mean ± SD. The independent *t* test was used. **P* < 0.001 for all domains. BP indicates Bodily Pain; GH, General Health; MCS, Mental Health Component Score; MH, Mental Health; PCS, Physical Health Component Score; PF, Physical Functioning; RE, Role-Emotional; RP, Role-Physical; SF, Social Functioning; VT, Vitality.

TABLE 4. PedsQL Scores (Patients' and Parents' Reports) for β-TM Patients on Different Iron Chelators

Age	DFO	DFX	Combined (DFO + DFX)	*P*
5-7 y old				
Physical Functioning				
Child	68.75 ± 8.84	75.43 ± 15.71	0	0.423
Parent	70.31 ± 7.86	72.92 ± 12.78	0	0.701
Psychosocial Health Summary Score				
Child	84.52 ± 4.05	86.96 ± 14.86	0	0.759
Parent	86.67 ± 6.09	87.99 ± 5.95	0	0.725
Total summary score				
Child	77.84 ± 14.30	86.08 ± 5.49	0	0.169
Parent	80.98 ± 6.49	82.34 ± 4.60	0	0.681
8-12 y old				
Physical Functioning				
Child	72.08 ± 24.56	72.87 ± 12.40	78.57 ± 20.68	0.732
Parent	72.71 ± 21.86	73.58 ± 15.54	80.45 ± 16.44	0.594
Psychosocial Health Summary Score				
Child	77.7 ± 18.45	76.99 ± 18.87	75.95 ± 20.52	0.766
Parent	73.10 ± 20.15	72.37 ± 20.64	75.50 ± 20.74	0.670
Total summary score				
Child	75.94 ± 17.96	75.28 ± 18.39	77.01 ± 20.11	0.868
Parent	73.36 ± 17.58	72.49 ± 17.84	77.59 ± 18.48	0.586

Values are expressed as the mean ± SD.
The independent *t* test was used for the scores of the 5- to 7-year-old age group. ANOVA test was used for the 8- to 12-year-old age group.
β-TM indicates β-thalassemia; DFO, deferoxamine; DFX, deferasirox; PedsQL, Pediatric Quality of Life.

TABLE 5. Univariate Analysis of Patient Variables Associated With PedsQL Scores

Variables	Total Summary Score	Physical Functioning	Psychosocial Health	Emotional Functioning	Social Functioning	School Functioning
Age						
5-7	83.33 ± 9.56	74.36 ± 14.89	86.15 ± 12.11	74.30 ± 18.87	88 ± 18.09	95.83 ± 7.93
8-12	76.96 ± 14.94	73.51 ± 18.34	78.33 ± 15.45	76.59 ± 19.28	86.14 ± 15.62	72.5 ± 20.96
P	0.158	0.844	0.109	0.634	0.654	< 0.0001
Sex						
Male	82.18 ± 11.99	76.90 ± 15.43	82.58 ± 14.81	78.84 ± 18.09	89.69 ± 16.82	81.19 ± 24.34
Female	75.89 ± 14.66	71.71 ± 17.97	78.46 ± 14.99	73.66 ± 19.58	86.85 ± 16.12	74.71 ± 19.19
P	0.104	0.205	0.323	0.270	0.406	0.277
Serum ferritin (ng/mL)						
< 2500	83.29 ± 12.48	76.89 ± 15.11	86.30 ± 14.04	82.78 ± 17.40	89.08 ± 17.72	82.69 ± 19.11
> 2500	76.74 ± 14.13	72.73 ± 17.71	78.09 ± 14.81	73.28 ± 19.11	87.56 ± 15.87	75.48 ± 21.89
P	0.124	0.345	0.083	0.068	0.675	0.290
Educational level of mother						
Illiterate	70.18 ± 14.87	62.50 ± 25.29	72.84 ± 13.14	71.67 ± 23.32	78.64 ± 25.92	59.29 ± 25.07
Primary	78.76 ± 12.14	75.99 ± 15.34	79.92 ± 11.55	75.20 ± 15.46	88.78 ± 12.54	80.33 ± 14.07
Secondary	79.46 ± 14.84	74.90 ± 15.66	81.03 ± 17.04	76.64 ± 21.07	89.28 ± 16.93	78.67 ± 22.70
Higher education	84.15 ± 7.35	78.13 ± 5.42	87.46 ± 8.47	83.33 ± 14.43	93.75 ± 7.22	88.33 ± 10.40
P	0.184	0.05	0.016	0.640	0.221	0.030
Educational level of father						
Illiterate	65.76 ± 16.85	59.37 ± 27.50	70.40 ± 15.15	73 ± 8.37	72.08 ± 26.38	66.25 ± 15.48
Primary	78.70 ± 12.82	72.54 ± 17.76	80.51 ± 12.66	73.15 ± 19.34	88.38 ± 15.13	71 ± 27.66
Secondary	76.38 ± 15.11	74.22 ± 14.98	78.14 ± 16.49	73.43 ± 22.84	85.63 ± 17.84	78.64 ± 19.71
Higher education	84.44 ± 10.03	79.23 ± 13.89	85.25 ± 14.02	83.38 ± 13.23	95.65 ± 7.09	84.64 ± 15.38
P	0.094	0.076	0.231	0.963	0.020	0.691
Iron chelation						
DFO	75.82 ± 17.27	71.38 ± 22.003	78.58 ± 17.02	72.76 ± 24.93	86.58 ± 17.31	75.79 ± 26.26
DFX	80.22 ± 9.36	74.12 ± 14.003	81.97 ± 11.99	76.63 ± 16.54	89.30 ± 14.33	81.03 ± 15.43
Combined	77.00 ± 20.11	78.57 ± 20.68	75.95 ± 20.52	78.57 ± 16.76	79.29 ± 29.64	65 ± 25.66
P	0.293	0.643	0.384	0.468	0.521	0.402

DFO indicates deferoxamine; DFX, deferasirox; PedsQL, Pediatric Quality of Life.

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TABLE 6. Univariate Analysis of the Patients' Variables Associated With SF-36v2 Dimensions.

Variables	PF	RP	BP	GH	VT	SF	RE	MH	PCS	MCS
Sex										
Male	63.50 ± 24.39	62.38 ± 22.04	60.58 ± 30.83	34.70 ± 18.85	61.38 ± 13.63	64.25 ± 24.53	60.64 ± 23.46	65.05 ± 12.88	57.63 ± 19.29	67.97 ± 18.26
Female	58.18 ± 24.42	57.33 ± 26.11	74.32 ± 17.43	33.82 ± 18.36	60.55 ± 14.79	62.72 ± 26.46	58.50 ± 24.08	68.47 ± 15.96	60.86 ± 16.05	63.70 ± 20.20
P	0.485	0.505	0.079	0.879	0.851	0.847	0.772	0.453	0.556	0.478
Serum ferritin (ng/mL)										
< 2500	78.85 ± 12.44	79.33 ± 21.56	83 ± 18.66	47.23 ± 16.04	68.62 ± 12.70	81.54 ± 18.36	76.64 ± 17.90	71.15 ± 13.87	70.21 ± 10.87	73.42 ± 16.06
> 2500	52.59 ± 23.97	50.94 ± 19.83	60.95 ± 25.26	28.41 ± 16.45	57.50 ± 13.48	55.34 ± 23.87	51.48 ± 21.81	64.91 ± 14.60	54.44 ± 17.86	62.29 ± 19.72
P	0.001	< 0.001	0.008	0.001	0.016	0.001	0.001	0.200	0.005	0.082
Educational level of mother										
Illiterate	53.33 ± 26.01	49.58 ± 29.26	57.08 ± 27.95	25.83 ± 15.94	55.21 ± 17.97	54.17 ± 32.27	46.38 ± 25.71	54.17 ± 8.01	49.21 ± 22.48	54.89 ± 20.09
Primary	53.75 ± 23.53	50.86 ± 17.92	68.59 ± 14.58	32.38 ± 16.44	55.47 ± 10.07	61.41 ± 21.18	52.35 ± 16.37	67.95 ± 14.32	56.13 ± 15.04	66.71 ± 17.43
Secondary	67.50 ± 24.01	67.81 ± 23.73	68.06 ± 32.33	39.69 ± 19.79	66.61 ± 13.98	65.30 ± 27.51	69.18 ± 25.79	70.94 ± 14.63	64.11 ± 17.96	68.46 ± 20.74
Higher education	72.50 ± 22.55	78.13 ± 25.77	79.38 ± 28.31	32.50 ± 23.63	68.75 ± 14.43	78.13 ± 21.35	69.23 ± 23.45	65 ± 15.81	68.13 ± 11.12	67.18 ± 20.19
P	0.259	0.055	0.605	0.426	0.058	0.518	0.075	0.106	0.193	0.527
Educational level of father										
Illiterate	59.17 ± 27.64	53.33 ± 25.82	61.25 ± 29.19	31.50 ± 16.78	55.21 ± 17.42	79.17 ± 27.003	51.83 ± 22.41	62.50 ± 9.35	50.29 ± 22.54	63.61 ± 17.08
Primary	68.57 ± 12.49	56.43 ± 27.50	70.36 ± 22.10	30 ± 20.82	58.21 ± 17.69	55.50 ± 23.89	53.57 ± 30.37	66.43 ± 19.09	62.75 ± 16.76	62.83 ± 26.50
Secondary	57.63 ± 27.64	58.75 ± 25.09	71.79 ± 23.95	38.16 ± 18.80	62.34 ± 12.70	63.22 ± 26.12	63.78 ± 23.48	69.86 ± 13.93	58.80 ± 16.51	68.94 ± 19.17
Higher education	62 ± 23.94	67.75 ± 20.08	62.25 ± 29.78	31.40 ± 18.03	63.63 ± 12.79	60 ± 23.003	60.19 ± 20.45	64 ± 15.42	63.33 ± 17.38	62.95 ± 16.49
P	0.791	0.654	0.716	0.673	0.629	0.372	0.648	0.642	0.508	0.819
Iron chelation										
DFO	53.18 ± 24.13	52.73 ± 19.57	58.93 ± 26.03	29.09 ± 19.43	56.88 ± 13.86	54.02 ± 21.87	50.23 ± 19.16	64.60 ± 13.43	52.63 ± 17.41	61.11 ± 18.66
DFX	78.57 ± 15.25	77.86 ± 23.10	87.86 ± 15.72	46.64 ± 11.73	70.23 ± 11.71	87.84 ± 13.55	81.64 ± 16.43	75.36 ± 13.79	74.13 ± 10.34	78.36 ± 14.88
Combined	46.67 ± 19.92	43.13 ± 13.78	53.33 ± 8.76	24.17 ± 12.42	54.17 ± 9.61	41.08 ± 9.38	41.98 ± 13.18	55.17 ± 9.17	49.33 ± 5.69	53.21 ± 15.91
P	0.001	0.001	< 0.001	0.005	0.007	< 0.001	< 0.001	0.007	< 0.001	0.005

BP indicates Bodily Pain; DFO, deferoxamine; DFX, deferasirox; GH, General Health; MCS, Mental Health Component Score; MH, Mental Health; PCS, Physical Health Component Score; PF, Physical Functioning; RE, Role-Emotional; RP, Role-Physical; SF, Social Functioning; SF-36v2, Short Form-36 health survey questionnaire, version 2; VT, Vitality

Caocci et al[7] reported that parents tended to underestimate their children's HRQoL, and they found that parents reported lower scores for Emotional Functioning, Psychosocial Health Summary, and the Total Summary score. This discrepancy in the findings of different studies supported the combination of children's self-reports and parents' proxy reports to investigate HRQoL in children.

In the patient group, there were no significant differences in PedsQL scores between male and female subjects. This result was similar to that reported by Thavorncharoensap et al[6] in Thailand, whereas Caocci et al[7] reported a significant difference in sex within the PedsQL School domain, in which girls had higher median scores than boys.

Regarding children aged 13 to 17 years old, the SF-36v2 questionnaire revealed significantly lower scores in all dimensions among patients with β-TM compared with the control group, with General Health being most affected. This result was similar to that of Porter et al,[11] who reported lower mean scores on all SF-36 domains, compared with age-matched individuals. However, Ismail and Campbell[23] reported similar results except for Bodily Pain and Role-Emotion, and they also reported that General Health was the most affected domain.

This study demonstrated that, among patients with β-TM aged 13 to 17 years old, there were no significant differences in any of the dimensions of SF-36v2 scores between male and female subjects. This finding was consistent with those of Baghianimoghadam et al[1] in Iran, who used the SF-20 for the assessment of HRQoL in thalassemic patients and did not report a significant difference in any domains of the SF-20 between male and female patients.

Thalassemia, as a chronic disease, negatively affects perceived Physical Functioning, Social Functioning, Bodily Pain, and General Health compared with the normal population. Assessment of HRQoL differs from other forms of medical assessment in that it focuses on the individual's own views of his or her well-being and also assesses other aspects of life, providing an overall view of well-being.[27] In general, the poor QoL of patients with β-TM probably results from a complex combination of living with a chronic disease and new challenges related to improved life expectancy with thalassemia.[21]

The current study did not report significant differences in PedsQL scores among different age groups and different iron chelators. This finding was in agreement with those of Torcharus and Pankaew[14] in Thailand and Ayoub et al[12] in Saudi Arabia.

Regarding the SF-36v2, there were significant differences in all domains relative to the type of ICT, with better HRQoL for the DFX group compared with other groups. Porter et al[11] reported that the mean SF-36 domain scores were generally higher following treatment with DFX and that they were closer to population norm scores for the UK general population and for patients previously receiving DFO therapy, although approximately 20% of the studied patients were younger than 16 years old.

The effect of injectable ICT on all of the patients was high, especially in adolescents and young adults with regard to being able to socialize with peers. In addition, the presence of bumps and bruises caused by injections restricts them from wearing certain clothes or from participating with others in recreational activities.[28]

Independent risk factors associated with HRQoL assessed by the PedsQL revealed that age was associated with School Functioning. Caocci et al,[7] in their study of thalassemic patients originating from different Middle East countries, including Iraq, and Torcharus and Pankaew,[14] in Thailand, did not report any associations with age. Ismail and Campbell[23] found that, for School Functioning by age, the scores of children with thalassemia remained low as they aged, and they claimed that repeated or frequent visits to hospitals for BTs affected this aspect.

A significant association between paternal education and Social Functioning was found in this study. In addition, maternal education was significantly associated with Physical, Psychosocial, and School Functioning. Kaheni et al[29] investigated education level and its correlation with QoL in thalassemic patients using the World Health Organization standard QoL questionnaire (WHOQOL-Bref), and they found significant correlations between parental education level and social relationships and physical health.

Significant associations of the type of ICT (all domains) and serum ferritin with all SF-36 scales, except for the Mental Health and Mental Component score, were observed in this study. Abetz et al[28] reported a significant effect of IOL and ICT on patients' daily lives from both the patients' and clinicians' perspectives because the consequences of IOL and nonadherence to ICT can result in severe morbidities, including cardiac disease, diabetes, failure of sexual development, osteoporosis, and liver damage leading to early mortality.

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