Health-Related Quality of Life of Omani Adult Patients with β-Thalassemia Major at Sultan Qaboos University Hospital, Muscat, Oman

Asma Al-Rushaidi[1], Sara Al-Hinai[2] and Hana Al-Sumri[3*]

[1]College of Medicine and Health Sciences, Sultan Qaboos University, Muscat, Oman

[2]College of Medicine and Health Sciences, Sultan Qaboos University, Muscat, Oman

[3]Department of Family Medicine and Public Health, College of Medicine and Health Sciences, Sultan Qaboos University, Muscat, Oman

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*Corresponding author: *alsumry@squ.edu.om*

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Abstract

Objectives: The impact of β-thalassemia major (β-TM) on health-related quality of life (HRQoL) in Oman is not yet known.. Affected individuals suffer from a wide range of physical, mental, and social consequences due to the need for regular hospital visits for blood transfusions and complications related to iron overload complications. This study aimed to assess the HRQoL of adult patients with β-TM attending a single tertiary care center in Muscat, Oman. Identifying the factors related to Omani patient's QoL will help enhance patient's management and counselling.

Methods: A cross-sectional study was conducted among adult patients (≥18 years) with β-TM at the Sultan Qaboos University Hospital between September and November 2022. A validated Arabic version of the self-reported 36-item Short-Form Health Survey was used to determine HRQoL.

Results: A total of 78 patients with β-TM were enrolled in the study, of which 53.8% were male and the mean age was 26±0.8 years ranging from 21 to 53 years. Majority of patients were from Al Batinah North region (n = 21; 26.9%) or Muscat (n = 20; 26%), unmarried (n = 44; 56.4%), did not have university-level educational qualifications (n = 45; 57.7%), and were unemployed (n = 44; 56.4%). The HRQoL domain with the highest score was role limitations due to emotional problems (median score: 100.0), while general health and vitality received the lowest scores (mean scores: 60.2 ± 15.9 and 59.1 ± 20.5, respectively). Several variables were associated with better HRQoL in certain domains, including being married, having a high level of education, being employed, exercising regularly, and receiving family support ($p \leq 0.05$). However, iron overload and having ≥3 β-TM-related disease complications were associated with poorer general health scores ($p = 0.031$ and 0.038, respectively), while a history of mental issues was associated with poorer scores in six out of eight HRQoL domains ($p \leq 0.05$). Moreover, negative perceptions regarding the social impact of the disease, including delayed marriage, workplace difficulties, and reduced academic achievement were associated with poorer HRQoL in various domains ($p \leq 0.05$).

Conclusions: Although the studied sample reported generally good quality of life, several factors were found to affect HRQoL in various domains. In particular, healthcare providers should prioritize the maintenance of acceptable iron overload levels in Omani patients with β-TM to help avoid the development of disease-related complications, thereby ensuring better control of their clinical condition and consequently improving their HRQoL.

Keywords: Beta-Thalassemia Major; Health-Related Quality of Life; Adults; Oman.

Introduction

β-thalassemia is an autosomal recessive hematological disorder characterized by the inadequate production of functional hemoglobin due to an abnormality in the genes that produce β chains of hemoglobin.[1] Based on the number of chains involved, β-thalassemia can be classified into three forms: minor, intermedia, and major, all of which vary in terms of clinical presentation and symptoms.[2] Of these, β-thalassemia major (β-TM) is considered the most serious and life-threatening, requiring regular lifelong blood transfusions to avoid chronic anemia.[3] However, numerous transfusions can lead to the development of iron overload, in which high levels of iron are deposited in various organs, potentially resulting in cardiac failure, diabetes mellitus, endocrine abnormalities, and renal and skeletal system complications.[2,4]

In comparison thalassemia minor is a thalassemia carrier state while thalassemia intermedia is a mild to moderate in severity with majority of patients not requiring blood transfusion. Therefore, they are not as severe as thalassemia major whom are blood transfusion dependent and thus are not included in this study.

As a result of the introduction of routine blood transfusion therapy coupled with recent advancement of iron-chelating medications as a standard management regimen, the life expectancy and survival of patients with β-TM worldwide has dramatically improved in recent decades.[5] However, in comparison with the general population and patients with other chronic non-communicable diseases, individuals with β-TM suffer significant impairment to their health-related quality of life (HRQoL).[6-9] Affected individuals suffer from a wide range of physical, mental, and social consequences due to the need for regular hospital visits for blood transfusions as well as a result of iron overload complications, including organ damage, liver and spleen enlargement, and changes to their physical appearance due to delayed growth and bone deformities of the face and skull.[10-12] Other challenges reported by patients include low self-esteem, stress, fatigue, reduced mental wellbeing, and difficulties fulfilling their personal and familial responsibilities and managing their illness.[13,14]

According to data from the Gulf Family Health Survey, the average prevalence of the β-thalassemia trait in Oman is ~2%, although this varies between different regions, with the highest prevalence rates identified in the North Al Batinah region (3.9%) and Muscat (2.8%).[15] The Hematology departments in hospitals located in the capital city Muscat including SQUH get patients referred to them from various regions in Oman with few hospitals providing care to patients in more distant areas. Although several previous studies from Oman have examined the quality of life of pediatric patients with β-TM, very few have targeted affected adults.[16,17] There is a need to evaluate factors that may affect the HRQoL of adult patients, especially the physical, psychological, and social consequences of the disease, in order to help healthcare providers improve treatment outcome and tailor counselling to these patients' specific needs. This study therefore aimed to evaluate the HRQoL of adult patients with β-TM in Oman as well as the effect of various sociodemographic, social, and clinical characteristics on HRQoL outcomes.

Methods

This prospective cross-sectional study was conducted at the Sultan Qaboos University Hospital (SQUH), a tertiary care institution located in Muscat, Oman, to which patients are referred from all over the country. The target population included all adult patients with β-TM who were followed-up at SQUH between September and November 2022. The inclusion criteria consisted of Omani patients aged ≥18 years with β-TM who were either attending appointments at the SQUH outpatient department (OPD) or visiting the day care unit to receive blood transfusions during the study period. Non-Omani patients, those under 18 years of age, patients diagnosed with β-thalassemia minor or intermedia, patients admitted to the hospital inpatient wards, and those who were in an unstable condition were excluded from the study.

The necessary sample size for the study was calculated based on the total number of Omani adult patients with β-TM who were followed-up at SQUH in 2022 (N = 100). Given the study's outcome measure as a mean of HRQoL scores, the sample size was calculated using the below formula for a finite population mean. Based on a previous study,[18] a standard deviation (SD) of 23.1 and a permissible error of 5% calculated from the mean score of 54.7, a sample size of 74 patients was required

$$n= [NxZ2x(SD)2] / [d2x(N-1)+Z2x(SD)2]$$

Data regarding the patients' HRQoL was determined using an Arabic version of the Medical Outcomes 36-item Short-Form Health Survey (SF-36).[18,19] The SF-36 is a rigorously tested questionnaire designed to evaluate HRQoL across eight distinct domains, encompassing the respondent's evaluations of their overall health, physical capabilities in work and daily life, vitality (indicating their levels of energy or fatigue), physical discomfort, emotional wellbeing, which includes feelings of contentment and anxiety, limitations in roles due to physical or emotional issues, social interactions, and personal perceptions of any health changes.[19]

There are two distinct concepts measured by the SF-36: a physical dimension and a mental dimension through the 8 domains. All scales do contribute in different proportions to the scoring of both physical and mental measures. The SF-36 is widely used for assessment of HRQoL in diverse settings and it has been found to be reliable and valid for measuring QoL of individuals with several chronic health conditions and in several countries.[19]

Each item in the questionnaire is represented as a single variable and scaled from 0 to 100 wherein a higher score is indicative of more favorable quality of life. The original English-language version of the SF-36 has been proven to act as a reliable measure of HRQoL, with Cronbach's alpha values ranging from 0.78–0.93.[20] The Arabic version was tested for internal consistency and reliability in a sample of adult Saudi Arabian citizens with sickle cell disease and showed good reliability across all eight domains (Cronbach's alpha value range: 0.6–0.86).[18]

An additional questionnaire was developed, consisting of two sections. The first section sought to determine the sociodemographic background of the participants, including their gender, age, place of residence, education level, and employment and marital status. The second section collected information related to the clinical and perceived social impact of the disease. This included information regarding the frequency of blood transfusions per month, average ferritin level within the last three months prior to the survey being administered, degree of compliance with iron-chelating medications, physical activity level, presence of other comorbid chronic diseases, and number of disease-related complications like hepatosplenomegaly, skin ulceration, growth retardation, and heart complications. The final version of the questionnaire was piloted among six patients prior to the study commencement to check for length, clarity, and appropriateness to be self-administered. The pilot study resulted in minor amendments in the sociodemographic and clinical information sections in order to enhance questions clarity, flow and to further ease data analysis.

Data were collected using a link to the online questionnaire distributed electronically by the researchers to the mobile devices of selected participants attending the hospital clinics. In addition, a quick response (QR) code to the online survey was generated and displayed in the OPD and day care units to be scanned by visiting patients. All participants received a study information sheet and were required to fill out an informed consent form.

All collected data were entered into and analyzed using the Statistical Package for the Social Sciences (SPSS) software (IBM Corp., Armonk, NY). The participants' demographic and clinical characteristics were presented as frequencies and percentages for categorical variables and as means and standard deviations or medians for continuous variables, depending on the normality of the data distribution. SF-36 scores were calculated and presented for each of the eight HRQoL domains as a mean or median score, according to the normality of data distribution determined using a simple Kolmogorov-Smirnov test. The scores of the domains of vitality and general health did not follow normal distribution while the scores of all the other 6 domains did follow a normal distribution . After checking the distribution pattern of the SF-36 scores, associations between various HRQoL domain scores and selected sociodemographic, clinical, and social impact characteristics were examined using appropriate tests of significance, including the independent student's t-test or Mann-Whitney U test for two independent samples for scores following normal and non-normal distribution respectively tested using the simple Kolmogorov-Smirnov test. For three or more independent samples, analysis of variance or Kruskal-Wallis tests were administered for scores following normal and non-normal distribution respectively tested using the simple Kolmogorov-Smirnov test. A p value of ≤ 0.05 was considered statistically significant.

Ethical approval was obtained from the Medical Research and Ethics Committee (MREC) of the College of Medicine and Health Sciences, Sultan Qaboos University (MREC #2782). Informed written consent was obtained from all participants prior to their taking part in the study.

Results

A total of 78 Omani adult patients with β-TM met the inclusion criteria, completed the distributed questionnaires, and were included in the analysis. The mean age of the respondents was 26 ± 0.8 years, with only three patients (3.8%) being over 45 years of age. Just over half of the patients (n = 42; 53.8%) were male. Most patients originated from the Al Batinah North region (n = 21; 26.9%) or Muscat (n = 20; 26%). In addition, the majority were unmarried (n = 44; 56.4%), did not have university-level educational qualifications (n = 45; 57.7%), and were unemployed (n = 44; 56.4%) [Table 1]. A considerable proportion of patients (n = 32; 41.0%) reported never exercising during the week.

Table 1: Characteristics of the studied Omani adult patients with β-thalassemia major (n = 78).

Characteristic		n (%)
Age group (years)	18–24	14 (17.9)
	25–34	43 (55.1)
	35–44	18 (23.1)
	>=45	3 (3.8)
Gender	Male	42 (53.8)
	Female	36 (46.2)
Married	Yes	34 (43.6)
	No	44 (56.4)
Place of residence	Muscat	20 (25.6)
	Al Batinah North	21 (26.9)
	Al Batinah South	6 (7.7)
	Ad Dhakhiliyah	9 (11.5)
	Al-Dhahirah	6 (7.7)
	Ash Sharqiyah North	8 (10.3)
	Ash Sharqiyah South	7 (9.0)
	Musandam	1 (1.3)
Education level	School	45 (57.7)
	University	28 (35.9)
	Higher	5 (6.4)
Employment status	Employed	24 (30.8)
	Self-employed	7 (9.0)
	Unemployed	44 (56.4)
	Retired	3 (3.8)
Hx of mental issues	Yes	38 (48.7)
	No	40 (51.3)
Type of mental issue	Anxiety	20 (25.6)
	Depression	11 (14.1)
	Sleep disturbances	7 (9.0)
	None	40 (51.3)

Hx = history.

In terms of clinical characteristics, the majority of patients required an average of three blood transfusions per month (n = 47; 60.3%) and were complaint with iron therapy (n = 70; 89.7%), the most frequent form of which was oral iron chelators (n = 65; 83.3%), followed by both oral and pump infusions of iron chelators (n = 10; 12.8%). In total, 35 patients (44.9%) reported iron overload and 14 (17.9%) reported having other chronic diseases besides thalassemia. In addition, 38 patients (48.7%) reported that their β-TM had caused mental issues, including symptoms of anxiety (n = 20; 25.6%), depression (n = 11; 14.1%), and sleep disturbances (n = 7; 9.0%).

Only 12 patients (15.4%) suffered from three or more β-TM-related complications. Overall, the most common complication was osteoporosis (n = 28; 35.9%) followed by delayed growth/development (n = 27; 34.6%), gum and dental problems (n = 20; 25.6%), splenomegaly (n = 18; 23.1%), craniofacial bone deformities (n = 14; 17.9%), and hepatomegaly (n = 10; 12.8%). A total of 30 patients (38.5%) had a history of splenectomy. Among the 15 female patients who were married, just under half (n = 7; 46.7%) reported experiencing pregnancy difficulties due to their β-TM.

Patients were asked a series of questions to determine the perceived social impact of the disease. A total of 12 patients (15.4%) reported having been bullied at school because of their illness, while 34 (43.6%) indicated that

β-TM had negatively affected their academic performance. Just under one-third of patients (n = 24; 30.8%) reported social limitations due to the disease. In addition, 25 patients (32.1%) claimed that their illness was a reason for delaying marriage, although only three patients (3.8%) reported that β-TM had caused marital issues and had affected their relationships with their children, respectively. A total of 31 patients (39.7%) stated that they had experienced issues in the workplace due to their diagnosis. However, the vast majority (n = 72; 92.3%) reported receiving family support regarding their medical condition [Table 2].

Table 2: Responses to social impact of the disease in the studied sample.

Item	n (%)*
Do you receive family support for your β-TM?	
Yes	72 (92.3)
No	6 (7.7)
Do you find that having β-TM has limited your social life?	
Yes	24 (30.8)
No	54 (69.2)
Were you bullied at school due to β-TM?	
Yes	12 (15.4)
No	65 (83.3)
If not yet married, was β-TM a reason for delaying marriage?	
Yes	25 (32.1)
No	31 (39.7)
If married, has β-TM caused any marital issues?	
Yes	3 (3.8)
No	39 (50.0)
If you have children, has β-TM negatively affected your relationship with them?	
Yes	3 (3.8)
No	34 (43.6)
Has β-TM negatively impacted your academic achievements (e.g., lower grades/failing)?	
Yes	34 (43.6)
No	43 (55.1)
Has β-TM caused you any problems or difficulties in the workplace?	
Yes	31 (39.7)
No	31 (39.7)

β-TM = β-thalassemia major. *Percentages were calculated from the total number of valid responses for each variable.

Of the eight HRQoL domains included in the SF-36 tool, role limitations due to emotional problems was found to have the highest score (median score: 100), followed by physical functioning (median score: 85), indicating that the patients reported generally high quality of life in these domains. On the other hand, the domains of general health and vitality were scored the lowest, with mean scores of 60.2 ± 15.9 and 59.1 ± 20.5, respectively, indicating poorer HRQoL in these domains [Table 3].

Table 3: Health-related quality of life scores* per domain among the studied sample..

HRQoL domain	Mean ± SD or median (IQR)
Physical functioning	85 (21)†
Role limitations due to physical health	75 (50)†
Role limitations due to emotional problems	100 (67)†
Vitality	59.1 ± 20.5
Emotional wellbeing	68 (36)†
Social functioning	75 (38)†
Pain/fatigue	77.5 (27)†
General health	60.2 ± 15.9

*HRQoL = health-related quality of life; SD = standard deviation; IQR = interquartile range. *Assessed using the 36-Item Short-Form Health Survey. †Scores for these domains were presented as medians (IQR) as the values were not normally distributed according to a simple Kolmogorov-Smirnov test.*

A bivariate analysis was conducted to determine associations between selected characteristics and scores for each of the eight individual HRQoL domains. A p-value of ≤0.05 was considered statistically significant. In terms of sociodemographic characteristics, being employed was associated with higher scores in the domains of role limitations due to physical function (p = 0.001) and role limitations due to emotional problems (p <0.001). Higher levels of education were also significantly associated with better scores in the domains of role limitations due to physical function (p = 0.045) and general health (p = 0.039). Married patients reported significantly better quality of life in the domains of social functioning (p = 0.049) and role limitations due to emotional problems (p = 0.013). Although female patients reported worse scores for physical functioning compared to male patients, this association did not cross the threshold for statistical significance (p = 0.053) [Table 4].

Table 4: Associations between selected sociodemographic variables and health-related quality of life domain scores* among Omani adult patients with β-thalassemia major (N = 78).

Variable		HRQoL domain, Mean ± SD or median†							
		Physical functioning	**Role limitations due to physical health**	**Role limitations due to emotional problems**	**Vitality**	**Emotional wellbeing**	**Social functioning**	**Pain/fatigue**	**General health**
Age (years)	18–25	31.7	40.8	35.9	56.2 ± 15.0	65.1 ± 18.9	33.2	73.8 ± 20.0	55.4 ± 15.6
	25–35	38.2	38.1	38.8	59.6 ± 22.6	69.1 ± 21.3	39.0	70.7 ± 22.2	62.5 ± 15.9
	35–45	36.6	46.1	40.0	60.9 ± 21.6	72.0 ± 19.6	43.8	75.0 ± 18.2	60.3 ± 16.7
	>45	48.5	14.0	37.7	55.0 ± 8.7	58.7 ± 33.3	25.5	50.8 ± 26.5	50.0 ± 10.0
	p value	0.683	0.103	0.947	0.914	0.672	0.369	0.316	0.339
Gender	Male	42.1	39.2	39.7	61.2 ± 19.8	69.7 ± 21.4	43.4	73.4 ± 22.5	39.0
	Female	32.6	39.8	37.5	57.4 ± 21.2	67.8 ± 20.1	34.3	69.9 ± 20.1	39.0
	p value	0.053	0.903	0.063	0.432	0.705	0.063	0.486	0.992
Marital status	Yes	40.1	43.8	45.0	60.0 ± 21.2	37.1	43.9	72.0 ± 19.0	63.3 ± 15.4
	No	34.5	36.2	33.5	58.5 ± 20.3	38.6	34.3	71.2 ± 22.9	57.8 ± 16.1
	p value	0.261	0.118	**0.013**	0.753	0.768	**0.049**	0.870	0.135
Education level	School	36.0	34.9	34.9	57.9 ± 18.5	35.4	35.4	39.3	33.6
	University	39.0	43.9	42.3	61.2 ± 23.6	43.9	40.9	36.9	46.2
	Higher	34.1	56.1	49.8	58.8 ± 25.6	27.3	55.1	41.4	49.3
	p value	0.806	**0.045**	0.128	0.821	0.166	0.152	0.875	**0.039**
Employment status	Employed	43.3	52.7	52.0	63.1 ± 24.1	72.6 ± 22.7	45.7	73.7 ± 18.2	63.3 ± 15.9
	Self-employed	30.3	20.4	21.3	53.3 ± 18.3	59.3 ± 23.4	22.3	63.3 ± 30.3	58.6 ± 13.5
	Unemployed	33.9	35.8	33.1	57.7 ± 19.6	67.4 ± 19.5	36.9	71.8 ± 20.4	59.4 ± 16.7
	Retired	41.2	32.5	43.3	63.3 ± 12.6	77.3 ± 20.1	39.8	66.7 ± 39.9	51.7 ± 7.6
	p value	0.293	**0.001**	**<0.001**	0.669	0.451	0.092	0.735	0.605
Nature of work	Fieldwork	81.3 ± 4.8	12.5	10.8	46.3 ± 11.1	14.0	15.0	54.4 ± 29.6	73.8 ± 16.5
	Office work	82.0 ± 16.8	18.2	17.2	67.3 ± 25.4	17.0	15.7	73.0 ± 20.2	58.6 ± 12.8
	Both	87.7 ± 8.8	14.4	14.9	58.5 ± 21.6	11.3	14.1	76.3 ± 17.1	62.5 ± 16.9

p value	0.512	0.315	0.192	0.263	0.239	0.889	0.203	0.220

*HRQoL = health-related quality of life; SD = standard deviation. *Assessed using the 36-Item Short-Form Health Survey. †Scores were presented as medians for values not following normal distribution.*

Various associations were observed between clinical and social impact characteristics and scores in certain HRQoL domains. Perceptions that the disease had contributed to delayed marriage was significantly associated with worse HRQoL in the domains of role limitations due to physical function ($p = 0.022$), role limitations due to emotional problems ($p = 0.040$), and social functioning ($p < 0.001$). In turn, the belief that β-TM had negatively affected patients' academic achievements was significantly associated with worse scores in the role limitations due to physical function ($p = 0.009$), role limitations due to emotional problems ($p = 0.039$), social functioning ($p = 0.012$), and general health ($p = 0.016$) domains. Perceived workplace difficulties were associated with poorer scores in the domains of role limitations due to physical function ($p = 0.038$) and social functioning ($p = 0.040$).

Patients who exercised three times or more per week reported significantly better quality of life in the physical function domain compared to those who exercised less frequently ($p = 0.046$). Patients who received family support scored better in the vitality ($p = 0.019$), emotional wellbeing ($p = 0.004$), and general health ($p = 0.020$) domains; in addition, significantly poorer scores for the general health domain were observed among patients who had iron overload ($p = 0.031$) and three or more complication due to their illness ($p = 0.038$). Moreover, a history of mental issues was associated with poorer scores in six out of eight HRQoL domains, including role limitations due to physical function ($p = 0.006$), role limitations due to emotional problems ($p = 0.026$), vitality ($p = 0.022$), emotional wellbeing ($p = 0.003$), social functioning ($p < 0.001$), and general health ($p < 0.001$) [Table 5].

Table 5: Associations between selected clinical and social impact variables and health-related quality of life domain scores* among Omani adult patients with β-thalassemia major (N = 78).

Variable		HRQoL domain, Mean score ± SD or median†							
		Physical functioning	**Role limitations due to physical health**	**Role limitations due to emotional problems**	**Vitality**	**Emotional wellbeing**	**Social functioning**	**Pain/fatigue**	**General health**
No. of β-TM-related complications	0	78.2 ± 15.8	40.1	36.6	57.6 ± 24.8	65.5 ± 22.4	42.8	68.2 ± 22.8	60.7 ± 16.9
	1	82.8 ± 19.0	42.3	41.9	60.6 ± 19.7	71.4 ± 17.0	40.3	75.8 ± 16.3	63.1 ± 13.8
	2	68.6 ± 25.8	40.3	39.6	59.6 ± 24.3	60.7 ± 27.6	35.3	72.1 ± 19.0	63.2 ± 16.9
	≥3	78.5 ± 19.6	30.1	32.1	56.8 ± 11.0	74.6 ± 19.2	-	66.0 ± 30.0	47.7 ± 14.6
	p value	0.235	0.410	0.495	0.940	0.322	0.247	0.459	**0.038**
Hx of developmental delay	Yes	32.4	35.0	38.4	32.9	62.6 ± 19.6	34.3	73.9 ± 21.7	56.7 ± 17.9
	No	39.5	41.9	38.6	39.3	71.8 ± 20.8	40.7	70.3 ± 21.0	62.1 ± 14.6
	p value	0.165	0.174	0.975	0.217	0.067	0.211	0.492	0.154
Hx of splenomegaly	Yes	31.4	39.9	33.0	60.3 ± 22.0	74.3 ± 14.7	31.9	78.2 ± 17.0	58.1 ± 18.7
	No	30.9	31.1	32.3	58.4 ± 20.8	65.5 ± 21.8	32.7	70.6 ± 21.7	60.9 ± 14.8
	p value	0.923	0.077	0.893	0.759	0.142	0.874	0.195	0.530
Hx of splenectomy	Yes	37.4	40.3	39.6	63.9 ± 18.7	71.1 ± 21.1	36.0	78.2 ± 17.0	58.1 ± 18.7
	No	36.7	39.0	37.8	56.5 ± 21.3	67.2 ± 20.6	40.1	70.6 ± 21.7	60.9 ± 14.8

	p value	0.891	0.790	0.699	0.145	0.424	0.415	0.195	0.530
Hx of iron overload	Yes	37.7	35.9	36.3	55.4 ± 21.1	68.1 ± 21.7	38.6	67.5 ± 24.0	56.0 ± 16.1
	No	35.6	41.6	39.4	63.0 ± 19.5	70.4 ± 18.6	37.5	75.4 ± 17.8	63.9 ± 15.1
	p value	0.664	0.240	0.493	0.118	0.627	0.820	0.105	**0.031**
Compliant with iron therapy	Yes	38.0	40.6	39.7	59.9 ± 21.0	69.4 ± 21.4	39.3	71.9 ± 21.4	60.1 ± 16.0
	No	27.9	29.8	26.6	52.1 ± 15.0	61.7 ± 11.3	31.1	67.9 ± 20.1	60.6 ± 16.4
	p value	0.227	0.178	0.095	0.350	0.357	0.329	0.634	0.936
Blood transfusions (no. per month)	0	51.6	42.6	46.1	55.0 ± 28.9	69.0 ± 27.6	46.6	33.9	62.5 ± 12.6
	1	51.4	52.8	36.9	66.0 ± 20.4	68.8 ± 24.2	48.4	54.3	65.0 ± 15.4
	2	26.6	43.9	39.6	57.1 ± 18.3	67.2 ± 19.1	33.5	34.7	57.3 ± 16.8
	3	33.7	33.7	35.9	62.1 ± 20.6	69.6 ± 21.7	36.9	37.6	61.0 ± 15.9
	4	46.7	32.2	29.2	35.0 ± 15.0	74.7 ± 12.9	24.2	19.7	60.0 ± 27.8
	p value	0.060	0.171	0.754	0.222	0.987	0.393	0.288	0.904
Hx of mental issues	Yes	33.0	32.6	33.3	53.2 ± 18.8	30.2	27.3	67.7 ± 23.3	52.7 ± 13.9
	No	40.5	46.1	43.4	64.2 ± 20.9	45.2	48.6	74.9 ± 18.7	67.1 ± 14.6
	p value	0.128	**0.006**	**0.026**	**0.022**	**0.003**	**<0.001**	0.138	**<0.001**
Family support	Yes	37.0	40.3	39.4	59.9 ± 21.0	70.5 ± 19.3	38.6	71.3 ± 21.3	61.4 ± 15.8
	No	36.9	30.3	25.9	48.0 ± 7.6	43.2 ± 26.1	36.8	74.5 ± 20.5	45.8 ± 9.7
	p value	0.992	0.272	0.139	**0.019**	**0.004**	0.852	0.746	**0.020**
Impact on social life	Yes	33.7	38.6	38.1	59.4 ± 21.1	65.7 ± 20.1	33.4	38.7	57.5 ± 17.6
	No	38.3	39.9	38.7	59.0 ± 20.5	70.0 ± 21.1	40.9	38.4	61.4 ± 15.1
	p value	0.400	0.806	0.901	0.948	0.398	0.149	0.960	0.321
Marriage delay	Yes	21.8	23.2	23.0	59.1 ± 14.6	66.7 ± 20.4	18.3	68.4 ± 20.9	55.4 ± 16.1
	No	29.5	32.8	31.1	59.0 ± 24.1	70.1 ± 20.9	35.5	77.3 ± 21.3	62.3 ± 14.4
	p value	0.066	**0.022**	**0.040**	0.985	0.548	**<0.001**	0.131	0.099
Workplace difficulties	Yes	28.3	27.0	28.3	56.7 ± 18.8	65.3 ± 19.9	26.1	27.3	58.6 ± 18.3
	No	29.7	36.0	32.7	63.4 ± 21.5	70.6 ± 23.6	34.9	33.5	62.7 ± 12.5
	p value	0.735	**0.038**	0.275	0.218	0.356	**0.040**	0.171	0.311
Reduced academic achievement	Yes	32.4	31.9	32.7	57.6 ± 17.5	32.2	31.2	68.6 ± 23.6	55.7 ± 16.2
	No	39.4	44.6	42.1	61.2 ± 22.1	41.6	43.4	73.9 ± 19.3	64.4 ± 14.4
	p value	0.158	**0.009**	**0.039**	0.453	0.061	**0.012**	0.281	**0.016**
Exercise frequency (no. per week)	0	38.7	39.3	38.4	61.1 ± 17.6	71.0 ± 17.6	40.9	73.3 ± 17.9	57.8 ±
	1	28.5	35.2	38.8	52.0 ± 21.5	59.3 ± 19.0	27.5	64.2 ± 23.2	55.9 ± 7.4
	2	21.9	29.1	26.4	59.5 ± 18.2	60.8 ± 27.8	35.9	73.3 ± 21.1	64.0 ± 16.5
	≥3	43.5	46.2	43.5	59.3 ± 25.3	73.4 ± 20.9	41.5	72.3 ± 24.2	63.8 ± 15.1
	p value	**0.046**	0.160	0.153	0.691	0.152	0.255	0.634	0.356

*HRQoL = health-related quality of life; SD = standard deviation; β-TM = β-thalassemia major; Hx = history. *Assessed using the 36-Item Short-Form Health Survey. †Scores were presented as medians for values not following normal distribution.*

Discussion

Patients with β-TM often undergo regular blood transfusions and may require other medical interventions. As patients with β-TM depend on regular blood transfusions for their survival, they tend to develop complications related to iron overload.[3] Better understanding of the HRQoL of affected individuals helps healthcare providers to evaluate the impact of these treatments on their daily lives, including potential side-effects and complications.[2,4] Moreover, chronic diseases like β-TM can have severe psychosocial and emotional implications.[13,14] As such, HRQoL-related research allows for a more nuanced understanding of how patients dealing with chronic, lifelong conditions like β-TM cope with the long-term impact of the disease and its treatment on various aspects of their lives. In addition, HRQoL is an important metric by which healthcare providers can identify areas for quality improvement and resource allocation purposes. It can inform strategies to enhance patient support, symptom management, and psychosocial care, leading to improved overall wellbeing, and can also aid in promoting a focus on comprehensive patient-centered outcomes as part of a holistic approach to medical care. The aim of the present study was to assess the HRQoL of adult patients with β-TM in Muscat, Oman. To the best of the authors' knowledge, there is a scarcity of research originating from Oman focusing on this topic, particularly among adults.

In the current study, adult patients with β-TM reported the lowest scores for general health (mean SF-36 score: 60.2 ± 15.9) and vitality (mean SF-36 score: 59.1 ± 20.5), thereby indicating that patients perceived themselves to have comparatively poorer quality of life in these HRQoL domains. In contrast, the highest scores were seen for role limitations due to emotional problems (median SF-36 score: 100) and physical functioning (median SF-36 score: 85). Nonetheless, it is important to note that the sample scored relatively highly in all eight domains when using a threshold score of 50 as to differentiate between lower and higher HRQoL.[19,21] A previous study from Bangladesh also noted that patients with β-TM reported relatively high physical functioning (mean SF-36 score: 72.47 ± 27.01); however, the next highest score was observed for bodily pain (mean SF-36 score: 71.52 ± 27.56), with the lowest scores seen for social functioning and general health.[6] Mean scores for the latter two domains (44.24 ± 23.33 and 48.19 ± 16.94, respectively) fell below the threshold, indicating that Bangladeshi patients experienced poorer HRQoL in these aspects.[6] Similarly, in a longitudinal cohort study of North American and UK patients, below-threshold scores were reported for all eight domains, of which the poorest were general health (41.5), role limitations due to emotional problems (46.78), and social functioning (46.79), while the best were bodily pain (49.41) and emotional wellbeing (49.04).[22] These findings indicate that patients with β-TM tend to report low scores for general health, with varying findings for other domains of HRQoL, perhaps due to varying population characteristics.

Indeed, certain sociodemographic factors were associated in the present study with higher scores in various HRQoL domains, including employment status, education level, and marital status. However, while female patients reported worse scores compared to males in the physical functioning domain, this association was not statistically significant ($p = 0.053$). In contrast, other researchers have reported that female patients with β-TM tend to have lower HRQoL in general, particularly in the domains of physical functioning, bodily pain, and role limitations due to emotional problems.[6,22] Given that female gender has been associated with lower HRQoL in the general population as well, and that the correlation reported above was on the borderline of statistical significance, it is possible that the lack of association seen in the present study was due to sample size or heterogeneity.[22,23] Further research is therefore needed to confirm whether gender has a significant impact on HRQoL among patients with β-TM in Oman.

The majority of patients in the present study had not attained higher educational qualifications (57.7%) and faced difficulties in securing a job (56.4%), likely because of their medical condition. In a previous study, Daar *et al.*[17] reported that adults with β-TM in Oman demonstrated significant impairments to their short-term working memory, executive functioning (i.e., verbal fluency), and verbal and auditory processing, all of which could impact their ability to secure employment as well as their academic and job performance. Indeed, over one-third of patients in the present study (43.6% and 39.7%, respectively) believed that their condition had impacted their academic achievements and caused them problems or difficulties in the workplace. Li *et al.*[24] reported that a similar proportion (40%) of adults with β-TM responding to a global survey were of the opinion that their condition often or always limited their career opportunities; moreover, 41.7%, 34.4%, and 19.5% of employed respondents admitted that their β-TM had resulted in productivity loss, impaired job performance, and absenteeism, respectively.

Pakbaz *et al*.[25] reported that fewer adults with β-TM in North America were able to secure full-time employment compared to the general population, despite there being no association between employment or educational achievement and transfusion or chelation requirements.

Nonetheless, despite the difficulties caused by their condition, patients who were employed in the current study showed significantly higher scores in the domains of role limitations due to physical function ($p = 0.001$) and role limitations due to emotional problems ($p < 0.001$), while patients with a university degree reported significantly better scores in the domains of role limitations due to physical function ($p = 0.045$) and general health ($p = 0.039$). Both employment status and education level have been reported as significant contributors to HRQoL in other β-TM-related research.[7,26,27] However, the belief that β-TM had negatively affected academic achievements was significantly associated with poorer scores in various domains of HRQoL in the current study, including general health, role limitations due to physical function and emotional problems, and social functioning ($p < 0.05$ each). Moreover, perceived workplace difficulties were associated with poorer scores in the domains of role limitations due to physical function ($p = 0.038$) and social functioning ($p = 0.040$).

Goulas *et al*.[28] suggested that patients who receive iron chelation regularly have fewer limitations in their ability to work and thus have higher HRQoL. Just under half (44.9%) of the patients in this study reported suffering from uncontrolled levels of iron overload (i.e., above 3,000 units); moreover, this factor was significantly associated with poorer scores in the general health domain in comparison to patients who had lower levels of iron overload ($p = 0.031$). However, compliance with iron-chelating medications was not found to significantly affect scores for any of the HRQoL domains. The most common disease-related complications reported by patients was osteoporosis (35.9%), followed by developmental delay (34.6%), which can be explained by multiple factors including bone marrow expansion, imbalanced cytokine profiles and the deposition of iron in the pituitary, thyroid, gonads, and other glands, resulting in hormone secretion deficiency and decreased peak bone mass.[29,30] In addition Unsurprisingly, patients who had three or more complications reported significantly lower scores in the general health domain of HRQoL ($p = 0.038$). In line with these findings, Sobota *et al*. also reported that a greater number of disease complications was associated with significantly lower HRQoL scores among patients from North America and the UK.[22] A study from Iran also reported that the presence of disease complications were linked with poorer quality of life among patients with β-TM.[31]

In the current sample, just under half (48.7%) of all patients reported a history of mental health problems, including symptoms of anxiety (25.6%), depression (14.1%), and sleep disturbances (9.0%). Studies from Iran and Lebanon have similarly reported high rates of anxiety, depression, and other mental health issues among patients with β-TM.[32,33] As is to be expected, a history of disturbed mental wellbeing, as perceived and reported by the patients, was negatively related to HRQoL in six out of eight domains, including emotional wellbeing, social functioning, general health, vitality, and role limitations due to physical health and emotional problems ($p < 0.05$ each). Moreover, patients who believed that their condition had contributed to a delay in their getting married scored significantly lower scores in the domains of social functioning and role limitations due to physical health and emotional problems. In contrast, married patients reported better scores in the domains of social functioning ($p = 0.049$) and role limitations due to emotional problems ($p = 0.013$). This may be because marital status has been hypothesized to play a protective role in quality of life, especially against the development of depressive symptoms and mental illnesses in late adulthood, factors strongly correlated to lower HRQoL.[34] In turn, patients who reported exercising three times or more per week scored significantly higher in the physical functioning domain compared to those who did not. Several studies have shown the benefits of regular exercise in improving β-TM-related laboratory variables as well as quality of life.[35,36]

The HRQoL of Omani adult patients with beta thalassemia major is not yet known . This study adds to the existing literature information on the Qol of this group of patients from Oman using a standardized and a valid HRQoL tool. It has extensively evaluated information on various sociodemographic, clinical and social characteristics of patients with β-TM to their HRQoL scores across the different domains of the SF-36 to better understand the factors that influence their perceived QoL and thus help better counselling of patients by their healthcare providers. This study is also subject to several limitations. While prospective cross-sectional studies can identify associations between variables, they do not establish causation. Moreover, the sample included patients seen at a single institution, thereby limiting the generalizability of the findings. Future research should consider conducting a multi-centric study to help overcome issues of data representativeness when assessing patients with β-TM in Oman. In addition, using standardized and validated tools to measure patients' mental status would provide a more accurate assessment of each patient's mental wellbeing compared to the subjective reports used in this study, which could have subjected the findings to bias.

Conclusion

Adult patients with β-TM in Oman reported generally high HRQoL, although the domains of general health and vitality were among the lowest scored domains, indicating poorer quality of life in these compared to other domains. Uncontrolled iron overload leading to disease complications was found to be linked with poor quality of life across many domains, affecting the patients' academic, social, and mental health status. Healthcare providers should emphasize the importance of patient compliance with iron chelation medications to help avert the more serious disease-related complications that could compromise the patient's quality of life. Moreover, given the study findings, healthcare providers are encouraged to regularly screen patients for mental health issues and advise them as to the benefits of regular physical activity.

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