ORIGINAL RESEARCH

Failure to replicate the internal structure of Greek-specific thalassemia quality of life instrument in adult thalassemia patients in Sabah

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Purpose: To study the validity and reliability of the Malay version of the Specific Thalassemia Quality of Life Instrument (STQOLI) in Sabah's adult thalassemia patients.

Patients and methods: This cross-sectional study was done at Thalassemia Treatment Centre, Queen Elizabeth Hospital in Sabah, Malaysia. Eighty-two adult thalassemia patients who fulfilled the inclusion and exclusion criteria were conveniently selected for participation in the study. The English version of STQOLI was translated into Malay by using forward and back translations. The content of the questionnaire was validated by the chief hematologist of the hospital. The construct validity of the 40-item questionnaire was assessed by principal component analysis with varimax rotation and the scale reliability was assessed by Cronbach's alpha.

Results: The study failed to replicate the internal structure of the Greek STQOLI. Instead, 12 factors have been identified from the exploratory factor analysis, which accounted for 72.2% of the variance. However, only eight factors were interpretable. The factors were iron chelation pump impact, transfusion impact, time spent on treatment and its impact on work and social life, sex life, side effects of treatment, cardiovascular problems, psychology, and iron chelation pill impact. The overall scale reliability was 0.913.

Conclusion: This study was unable to replicate the internal structure of the Greek STQOLI in Sabah's adult thalassemia patients. Instead, a new structure has emerged that can be used as a guide to develop a questionnaire specific for adult thalassemia patients in Sabah. Future research should focus on the eight factors identified from this study.

Keywords: STQOLI, validity, reliability, Malay, transfusion

Introduction

Beta thalassemia, an inherited blood disorder, is most common in persons of Mediterranean, African, and Southeast Asian descent.[1] In Malaysia, the prevalence of the heterozygous carriers for the disease is reported to be about 4.5%.[2] The Malaysian Thalassemia Registry 2009 shows that one-fourth of the registered thalassemia patients are from the east Malaysia state of Sabah.[3] And it was estimated that over 1,000 cases are transfusion-dependent beta thalassemia patients.[4]

Beta thalassemia is a serious life-limiting condition[5] that not only affects patients' physical functioning but also their emotional functioning, social functioning, and school functioning, leading to impaired health-related quality of life (HRQOL) of the patients.[6] HRQOL is an important dimension of care[7] and can be seen as a way for assessment of patients' perspectives about their disease and related treatments, their perceived needs for health care and their preference for treatment and disease outcomes.[8]

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The HRQOL should be considered as an important index of effective health care as it can give a more holistic view of well-being.[9] However, there is very little published work on evaluation of HRQOL in thalassemia patients.[10,11] It is believed that the HRQOL in thalassemia patients is lower than that of normal population because of a variety of issues like the presence of comorbid conditions, frequent hospital visits for transfusion, painful injections, appearance, absence of sexual development, infertility, inability to take care of their own family, disease complications, uncertainties about the future, psychiatric disorders, and difficulties in employment and playing a role in society.[12]

A 36-Item Short Form Health Survey (SF-36) and its derivative were the most commonly used instrument to measure HRQOL in adult thalassemia patients. It may, however, be insensitive to the unique experience of thalassemia patients.[11] In 2012, Specific Thalassemia Quality of Life Instrument (STQOLI) was developed and had been validated for use among the patients in Greece.[11] So far, it is the only instrument that is tailored specifically for the adult thalassemia patients.

This study attempted to replicate the psychometric structure of the original STQOLI using the Malay version of the instrument.

Material and methods
Participants and settings
This cross-sectional study was conducted among adult beta thalassemia patients who received transfusion treatment at the Thalassemia Treatment Centre (TTC) in Queen Elizabeth Hospital from February to July 2015. Queen Elizabeth Hospital is a referral tertiary hospital located in Kota Kinabalu, the capital city of Sabah. The inclusion criteria were patients diagnosed with beta thalassemia and aged 18 years and above. The exclusion criteria were patients who do not understand Malay language or unwilling to participate in the study. The eligible patients were identified from the list of patients who received their transfusion treatment at the TTC. Eighty-two participants were conveniently selected during the transfusion day. The participants were justified as representative of all Sabah beta thalassemia patients as TTC caters not only for patients from Kota Kinabalu but also patients from other districts in Sabah. The study has been approved by Medical Research and Ethics Committee (MREC) of Malaysia.

Study instrument
In this study, HRQOL assessment was performed using the Malay version of STQOLI.[11] A user agreement was signed with the copyright owner of the original STQOLI,

Dr Georgios Lyrakos, from the Lyrakos G. Psychometrics and Research, Greece, prior to the use of the questionnaire.

The questionnaire consists of four domains: disease and symptoms (12 items), chelation therapy (13 items), psychosocial impact (10 items), and transfusion impact (5 items). The HRQOL was assessed by patient response in each domain. Both overall HRQOL and subscales were measured with a scale from 0 to 100, with higher values indicating better quality for each scale.

The translation of the English version STQOLI into the Malay version was done by the International Translation Network, a translating agency, using the forward-translation and back-translation. The content validity of the questionnaire was confirmed by the chief hematologist of the hospital.

Data collection
All eligible patients were approached as they came in for routine follow-ups at the TTC. Written informed consent was obtained prior to participation in the study. The administration of the questionnaire was done either via a face-to-face guided interview for those who cannot read or self-administration for those who can read. For the interview, the questions were read out word-by-word from the questionnaire and their responses were recorded. Only one trained interviewer was assigned for the interview.

Data analysis
Data were analyzed by IBM SPSS version 20.0 (IBM Corporation, Armonk, NY, USA). The sampling adequacy was assessed by Kaiser–Meyer–Olkin Measure of Sampling Adequacy. The internal structure of the questionnaire was assessed by principal component analysis with an orthogonal (varimax) rotation. Variables with eigenvalue more than 1 and factor loading more than 0.4 were retained. The reliability of the questionnaire was assessed by Cronbach's alpha coefficient. The participants' characteristics were presented by descriptive statistics.

Results
Eighty-two out of 147 thalassemia major patients aged 18 years and above were included in the study (56% participation rate). The reasons for exclusion were unable to understand the questions in Malay language (63 patients) and unwillingness to participate (2 patients). The participants' characteristics are shown in Table 1. The appropriateness of the factor analysis was assessed by the Kaiser–Meyer–Olkin Measure of Sampling Adequacy. The Kaiser–Meyer–Olkin Measure of Sampling Adequacy was 0.635, which is acceptable.[13] The Cronbach's alpha coefficient for the total

Table 1 Demographic data of the participants (n=82)

	Frequency (%)	Mean (SD)
Age (years)		23.4 (4.2)
Sex		
Male	42 (51.2)	
Female	40 (48.8)	
Iron chelation		
Oral pill only	21 (25.6)	
Subcutaneous only	3 (3.7)	
Combination	58 (70.7)	
Level of education[a]		
No formal education	8 (9.8)	
Primary	13 (15.9)	
Secondary	49 (59.8)	
Tertiary	12 (14.8)	
Residence		
Inside Kota Kinabalu	21 (25.6)	
Outside Kota Kinabalu	61 (74.4)	

Note: [a]Primary is years 7–12, secondary is years 13–17, tertiary is university program.
Abbreviation: SD, standard deviation.

scale was 0.913, which is excellent.[13] The factors, loadings and factors' labels after rotation are shown in Table 2. The analysis identified 12 factors accounting for 72.2% of the variance. The first factor accounted for the largest variance at 24.2% and the twelfth factor accounted for the smallest variance at 2.6%. Only eight factors were interpretable. The eight factors were "iron chelation pump impact" (component 1: q7, q29, q51, q25, q28, q8, q6), "transfusion impact" (component 2: q43, q45, q17, q44), "time spent on treatment and its effect on work and social life" (component 3: q46, q47, q20, q19, q50, q16), "sex life" (component 4: q39, q38, q36), "side effects of treatment" (component 5: q9, q34, q30), "cardiovascular problems" (component 6: q35, q32, q33), "psychology" (component 8: q2, q48, q49), and "iron chelation pill impact" (component 9: q12, q14). The scale reliability of each interpretable factor was assessed by Cronbach's alpha, with value 0.7 and higher was considered acceptable.[13] The Cronbach's alpha was highest for component 1 ("iron chelation pump impact") at 0.847 and lowest for the component 8 ("psychology") at 0.592. The factors with Cronbach's alpha less than 0.7 were the component 8 ("psychology") and the component 6 ("cardiovascular problems"). The Cronbach's alpha of the component 6 ("cardiovascular problems") and the component 4 ("sex life") can be improved by removing q33 (I feel fatigue when I have low hemoglobin) and q36 (splenectomy affects me negatively), respectively, both of which were irrelevant to the factors they belong to.

Discussion

The best HRQOL instrument is the one that shows consistent internal validity and constructs across different populations.

The replicability of factor structure of an instrument can be demonstrated by using the exploratory factor analysis. In this application, strong replication across cultures and languages not only confirms the goodness of the translations of the instrument, but also the universality of the factor structure. Without a reasonable likelihood of replicability, the researchers have little reason to use a particular scale of the instrument.[14]

The purpose of this study was the adaptation and validation of the Malay version of the STQOLI. The STQOLI is a tool that specifically measures the quality of life of adult thalassemia major patients. This study was unable to replicate the internal structure of the Greek version of the STQOLI (Table 3) in the Sabah's adult thalassemia patients. While exhibiting a different internal structure than the Greek version, the Malay STQOLI has the potential to be modified into a good tool to measure the quality of life of the adult thalassemia major patients in this region.

In comparison to the study by Lyrakos et al,[11] our sample was younger (mean age 23.4 vs 37.2 years), consisted of more males (51.2% vs 26.6%), less educated (14.8% vs 51.6% with tertiary education), and none of them were married (0% vs 37.5% married). The differences in these cultural constructs especially the education level may explain in part the variation in the internal structures between the two studies.

The difference in structure can also be attributed to the ambiguity of the purported factors described by Lyrakos et al,[12] which can be interpreted in many ways. For example, the study showed that the Greek thalassemia patients were able to distinguish between the concepts of "pain" (q28, q29) and "chelation impact of iron chelation pump" (q51, q6, q8, q7, q15). The Sabah's thalassemia patients, meanwhile, treated "pain" as part of the latter concept and were logically not wrong. Another notable example was that the Greek patients treated items about time spent for treatment (q46, q47) as a different concept from items about social and work life (q20, q19, q16). The Sabah's patients, however, seemed to think that the social and work life and time spent for treatment were indistinguishable.

It must also be mentioned that the Greek version of STQOLI was originally designed for self-administration. In our study, some participants need to be interviewed in answering the questionnaire due to the low literacy level. This may inadvertently affect the results of the study as the participants might not respond truthfully because they might wish to present themselves in acceptable manner. Meanwhile, the importance of literacy for self-reported health-related quality of life was highlighted by Cassis et al.[15] It was reported that education level was not found to be a helpful criterion and thus an assessment of literacy level should be conducted

Table 2 Exploratory factor analysis with varimax rotation for the 40 items

Factor label	Item	Description	EFA Component											
			1	2	3	4	5	6	7	8	9	10	11	12
ICP impact	q7	I cannot sleep well because of the ICP	0.790											
	q29	Iron chelation procedure is painful to me	0.729											
	q51	The ICP troubles me	0.727											
	q25	The body imprints (eg black spots in the belly from the iron chelation machine or the color on the skin) makes me feel uncomfortable	0.682											
	q28	The intake of iron chelation drugs causes me painful abdominal discomforts	0.681											
	q8	QoL is affected by the time required by the iron chelation therapy with ICP	0.667											
	q6	I lost valuable time to prepare the ICP	0.506											
Transfusion impact	q43	The lack of blood units for my transfusion regime affects my emotional status negatively		0.688										
	q45	The distance between my home and the thalassemia center creates a problem in my daily life		0.638										
	q17	I am treated differently (negatively) in my workplace when they are aware about my disease		0.621										
	q44	I experience reactions from the blood transfusion, which affects the general state of my health		0.620										
Time spent on treatment and its effect on work and social life	q46	The time that I miss for the transfusion affects my life			0.764									
	q47	The time that I miss for the tests affects the quality of my life			0.713									
	q20	The disease limits my professional activities (work or school)			0.532									
	q19	I cannot go out with my friends as much as I would like to because of the disease			0.494									
	q50	I am energetic			0.466									
	q16	The time schedule of the intake of ICT affects my social life			0.458									
Sex life	q39	My sexual life is affected negatively because of the disease				0.867								
	q38	My sexual life is affected negatively because of the iron chelation therapy				0.809								
Side effects of treatment	q36	Splenectomy affects me negatively				0.703								
	q9	The per os chelation therapy causes me other side-effects					0.769							
	q34	I feel somnolence because of the iron chelation					0.654							
	q30	I suffer from arthralgias					0.527							
Cardiovascular problems	q35	I have arrhythmias because of the disease						0.840						
	q32	I have cardiological problems because of the disease						0.607						
	q33	I feel fatigue when I have low hemoglobin						0.531						

Factor label	Item	Description	1	2	3	4	5	6	7	8	9	10	11	12
Not interpretable	q31	I have osteoporosis problems because of the disease							0.725					
	q23	Some features in my appearance have been changed, a fact that bothers me							0.513					
Psychology	q15	My social relationships are affected by the ICP							0.447					
	q2	My emotional status restricts my everyday life								0.764				
	q48	I feel calm and peaceful								0.723				
	q49	I feel hopeless and depressed								0.436				
Iron chelation pill impact	q12	The amount of tablets for iron chelation troubles me									0.731			
	q14	The way of administration of ICT affects my nutrition									0.709			
Not interpretable	q41	Disease complications affect QoL										0.828		
	q13	The disease affects my ability to eat or drink whatever I want										0.421		
Not interpretable	q42	The origin of the blood (if it is substantially checked) that I will receive causes me anxiety and fear											0.640	
	q37	I entered puberty late due to the disease, which affects me negatively											0.533	
Not interpretable	q24	I prefer that others not know about my disease												0.742
	q40	I feel tired because of the disease												0.468
		Eigenvalue	9.685	3.231	2.303	2.206	1.948	1.648	1.581	1.519	1.426	1.224	1.085	1.031
		Cumulative %	24.21	32.39	38.05	43.56	48.43	52.55	56.51	60.31	63.87	66.93	69.64	72.22

Abbreviations: EFA, exploratory factor analysis; ICP, iron chelation pump; ICT, iron chelation tablet; QoL, quality of life.

Table 3 Internal structure of the Greek STQOLI

Factor label	Item	Description	EFA										
			Component										
			1	2	3	4	5	6	7	8	9	10	11
Chelation impact ICP	q51	The ICP troubles me	0.961										
	q6	I lose valuable time to prepare the ICP	0.955										
	q8	QoL is affected by the time required by the iron chelation therapy with ICP	0.945										
	q7	I cannot sleep well because of the ICP	0.926										
	q15	My social relationships are affected by the ICP	0.924										
Disease effect in mobility and social relations	q41	Disease complications affect QoL		0.732									
	q40	I feel tired because of the disease		0.731									
	q20	The disease limits my professional activities (work or school)		0.616									
	q19	I cannot go out with my friends as much as I would like to because of the disease		0.588									
	q30	I suffer from arthralgias		0.544									
	q49	I feel hopeless and depressed		0.521									
	q31	I have osteoporosis problems because of the disease		0.503									

(Continued)

Table 3 (*Continued*)

Factor label	Item	EFA Component										
		1	2	3	4	5	6	7	8	9	10	11
Chelation impact ICT	q12	The amount of tablets for iron chelation troubles me		0.811								
	q14	The way of administration of ICT affects my nutrition		0.772								
	q9	The per os chelation therapy causes me other side-effects		0.746								
	q16	The time schedule of the intake of ICT affects my social life		0.728								
Daily activity time	q46	The time that I miss for the transfusion affects my life			0.861							
	q47	The time that I miss for the tests affects the quality of my life			0.775							
	q45	The distance between my home and the thalassemia center creates a problem in my daily life			0.703							
Psychological quality	q50	I am energetic				0.875						
	q2	My emotional status restricts my everyday life				0.788						
	q48	Feel calm and peaceful				0.747						
Effect of chronicity	q35	I have arrhythmias because of the disease					0.709					
	q23	Some features in my appearance have been changed, a fact that bothers me					0.617					
	q32	I have cardiological problems because of the disease					0.608					
	q13	The disease affects my ability to eat or drink whatever I want					0.498					
Effect in sexual life	q38	My sexual life is affected negatively because of the iron chelation therapy						0.757				
	q39	My sexual life is affected negatively because of the disease						0.740				
	q37	I entered puberty late due to the disease, which affects me negatively						0.684				
Pain and fatigue	q33	I feel fatigue when I have low hemoglobin							0.752			
	q28	The intake of iron chelation drugs causes me painful abdominal discomforts							0.648			
	q29	Iron chelation procedure is painful to me							0.513			
Transfusion impact	q44	I experience reactions from the blood transfusion, which affects the general state of my health								0.306		
	q43	The lack of blood units for my transfusion regime affects my emotional status negatively								0.872		
	q42	The origin of the blood (if it is substantially checked) that I will receive causes me anxiety and fear								0.532		
Body image	q24	I prefer that others not know about my disease									0.728	
	q17	I am treated differently (negatively) in my workplace when they are aware about my disease									0.582	
	q25	The body imprints (eg, black spots in the belly from the iron chelation machine or the color on the skin) makes me feel uncomfortable									0.416	
	q36	Splenectomy that affects me										0.787
	q34	I feel somnolence because of the iron chelation										-0.529

Note: Copyright ©2012. Dove Medical Press. Adapted from Lyrakos G, Vini D, Aslani H, Drosou-Servou M. Psychometric properties of the specific thalassemia quality of life instrument for adults. *Patient Prefer Adherence.* 2012;6:477–497.[11]

Abbreviations: EFA, exploratory factor analysis; ICP, iron chelation pump; ICT, iron chelation tablet; QoL, quality of life; STQOLI, Specific Thalassemia Quality of Life Instrument.

prior to recruitment and those with limited literacy should be assisted to ensure the comprehension of the questions.[15]

The results of this study showed that the Malay version of STQOLI needs to be modified to suit the local population. The modification of the questionnaire should be based on the eight interpretable factors found in this study. Furthermore, concurrent validity should also be examined in future research. This can be done by administering another quality of life tool together with the modified instrument and the correlation between the two instruments should be assessed. One notable limitation of this study was the small sample size. This, however, was unavoidable as many of the thalassemia patients in Sabah are illiterate and had to be excluded from the study.

Conclusion

This study was unable to replicate the internal structure of the Greek STQOLI in Sabah's adult thalassemia patients. Instead, a new structure has emerged that can be used as a guide to develop a HRQOL questionnaire specific for adult thalassemia patients in Sabah. Future research in this area should focus on the eight factors identified from this study.

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Author contributions

All authors contributed toward data analysis, drafting and critically revising the paper and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Muncie HL, Campbell J. Alpha and beta thalassemia. *Am Fam Physician*. 2009;80(4):339–344.
2. George E, Jamal AR, Khalid F, Osman KA. High performance liquid chromatography (HPLC) as a screening tool for classical beta-thalassaemia trait in Malaysia. *Malays J Med Sci*. 2001;8(2):40–46.
3. Guidelines Development Group. *Management of Transfusion Dependent Thalassaemia*. 1st ed. Putrajaya: Ministry of Health Malaysia; 2009.
4. Teh KL, George E, Lai MI, Tan JAM, Wong L, Ismail P. Molecular basis of transfusion dependent beta-thalassemia major patients in Sabah. *J Hum Genet*. 2014;59:119–123.
5. Caocci G, Efficace F, Ciotti F, et al. Health related quality of life in Middle Eastern children with beta-thalassemia. *BMC Blood Disord*. 2012;12(6):1–7.
6. Thavorncharoensap M, Torcharus K, Nuchprayoon I, Riewpaiboon A, Indaratna K, Ubol B. Factors affecting health-related quality of life in Thai children with thalassemia. *BMC Blood Disorders*. 2010;10(1): 1–10.
7. Gollo G, Savioli G, Balocco M, et al. Changes in the quality of life of people with thalassemia major between 2001 and 2009. *Patient Prefer Adherence*. 2013;7:231–236.
8. Baghianimoghadam MH, Sharifirad G, Rahaei Z, Baghianimoghadam B, Heshmati H. Health related quality of life in children with thalassaemia assessed on the basis of SF-20 questionnaire in Yazd, Iran: a case-control study. *Cent Eur J Public Health*. 2011;19(3):165–169.
9. Telfer P, Constantinidou G, Andreou P, Christou S, Modell B, Angastiniotis M. Quality of life in thalassemia. *Ann N Y Acad Sci*. 2005; 1054:273–282.
10. Azarkeivan A, Hajibeigi B, Alavian SM, Lankarani MM, Assari S. Associates of poor physical and mental health-related quality of life in beta thalassemia-major/intermedia. *J Res Med Sci*. 2009;14(6):349–355.
11. Lyrakos G, Vini D, Aslani H, Drosou-Servou M. Psychometric properties of the specific thalassemia quality of life instrument for adults. *Patient Prefer Adherence*. 2012;6:477–497.
12. Haghpanah S, Nasirabadi S, Ghaffarpasand F, et al. Quality of life among Iranian patients with beta-thalassemia major using the SF-36 questionnaire. *Sao Paulo Med J*. 2013;131(3):166–172.
13. Coakes SJ. *SPSS Version 20.0 for Windows Analysis without Anguish*. 1st ed. Australia: John Wiley & Sons Australia Ltd; 2013.
14. Osborne JW, Fitzpatrick DC. Replication analysis in exploratory factor analysis: what it is and why it makes your analysis better. *PARE*. 2012;17(15):1–8.
15. Cassis FR, Carneiro JD, Villaca PR, et al. Importance of literacy for self-reported health-related quality of life: a study of boys with haemophilia in Brazil. *Haemophilia*. 2013;19(6):866–869.