The Relationship Between Socio-Demographic And Illness-Related Variables With The Quality Of Life Among Malaysian Adolescent With Thalassaemia: A Multi-Centre Study
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ORIGINAL ARTICLE

THE RELATIONSHIP BETWEEN SOCIO-DEMOGRAPHIC AND ILLNESS-RELATED VARIABLES WITH THE QUALITY OF LIFE AMONG MALAYSIAN ADOLESCENT WITH THALASSAEMIA: A MULTI-CENTRE STUDY

Azizah Othman[1], Qarem Mohamed Mustafa[2], Ariffin Nasir[1], Norsarwany Mohamad[1], Nurul Shafira Adi[1], Nurul Ilyana Hashim[1], Bin Alwi Zilfalil[3]

1. Department of Pediatrics, School of Medical Sciences, Universiti Sains Malaysia, 16150 Kelantan, Malaysia.
2. Department of Psychology, KIRKHS, International Islamic University Malaysia, 53100 Selangor, Malaysia.
3. Human Genome Centre, School of Medical Sciences, Universiti Sains Malaysia, 16150 Kelantan, Malaysia.

Abstract

Thalassaemia is a life-long illness that exists globally. The quality of life of adolescents with thalassaemia could differ based on the health policies of a specific region, existing level of socio-economic development and the illness related variables. This study examines the relationship between socio-demographic and disease-related variables with the quality of life among adolescents with thalassaemia involving multiple treatment centers spread throughout various locations in Malaysia. Participants included 218 adolescents (male=108; female 112) with mean age of 13.86 (SD=2.40). They completed the questionnaire consisting of demographic information, illness-related variables, and Pediatric Quality of Life Inventory 4.0 (PedsQL). The participants in this study was found to have higher total summary score (Mean = 69.64, SD = 14.03), psychosocial health (Mean = 70.23, SD = 14.91), emotional (Mean = 72.12, SD = 20.66), social (Mean = 79.82, SD = 17.37), and school (Mean = 58.69, SD = 16.77) functioning but with lower physical health (Mean = 68.50, SD = 17.22) as compared to previous study that was done in Kuala Lumpur. Findings also shows a significant positive correlation between level of education and frequency of hospitalization ($r = .156$, $p < 0.05$), frequency of transfusion ($r = .152$, $p < 0.05$), and physical health ($r = .186$, $p < 0.01$). An increase in the frequency of transfusion was found to significantly increase social functioning ($r = .137$, $p < 0.05$). Other significant correlations are discussed in addition to the quality of life experienced by patients with thalassaemia in different region of the world.

Keywords: Thalassaemia, Adolescent, Illness-Related Variables, Transfusion, Quality of Life
Corresponding Author: Assoc. Prof. Dr. Azizah Othman, Department of Pediatrics, School of Medical Sciences, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia
Tel: +609-767 6532

Email: azeezah@usm.my

Introduction

Thalassaemia is a life-long illness due to hereditary anemia from defects in hemoglobin production [1]. Malaysia Thalassaemia Registry reported that as of 2009, a total of 3,310 patients are registered as having beta-thalassaemia (β-thalassaemia) while an estimated of 600,000 to 1,000,000 individuals are carriers of thalassaemia in Malaysia. The numbers of individuals with thalassaemia are increasing throughout the years [2] and as such greater emphases are being placed on the identification of genetic markers of thalassaemia for treatment and preventative purposes [3]. Additionally, various medications with high efficacy have been produced to reduce the mortality and morbidity related to thalassaemia [4]. The current focus on optimal clinical management is not only towards the management of the symptoms but has also been shifted to the physical health, psychosocial health, and the overall quality of life (QoL) of patients with thalassaemia. Ismail *et al.* [5] found that the QoL for children with thalassaemia in Malaysia is significantly lower than their healthier counterparts. This is due to how the illness impacts their school performance, self-image, financial problems, and their ability to integrate with the society [6]. Previous studies also found that individuals with β-thalassaemia had a significantly lower QoL as compared to their healthier counterparts [6, 5].

The poor QoL experienced by patients with thalassaemia can be explained by disease-related variables and demographic factors such as frequency of hospitalization, onset of illness, and social economic status [7, 8]. However, the predictors of the QoL for patients with thalassaemia may differ based on the cultural differences and the health policies of the respective region [9]. In Thailand, age of patients and household income were found to be significant predictors of QoL [8] which differs from Malaysia in which age and household income are not significant predictors for the QoL [5]. Although a study in India found that age is a significant predictor of QoL, no other socio-demographic variables were found to be a significant predictor [10]. Elalfy and colleagues [11] on the other hand found that the predictors of QoL for patients with thalassaemia in Egypt are pretransfusion hemoglobin (Hb) and serum ferritin (SF). Similarly, a study that examined the QoL of multiple countries in Middle East (Kurdistan, Libya, Palestine, Syria, and Iraq) found that the start of iron chelation is associated with the QoL of patients with thalassaemia [12]. Early start of treatment and the adherence to the treatment itself was found to be significantly associated with individual's QoL [13 – 15]. These suggest the experience of patients with thalassaemia differs in different country with various factors affecting the QoL.

Therefore, it is important to consider the health policies of a specific region, existing level of socio-economic development and the illness related variable in examining the relationship between patients QoL [9]. The aim of this research is to examine the relationship between socio-demographic and disease-related variable with the QoL among adolescents with thalassaemia particularly in Malaysia. This research involves multiple treatment centers spread throughout various locations in Malaysia as compared to a

single-location study. It is hypothesized that: (i) adolescents with thalassaemia experiences lower QoL; (ii) there is a positive relationship between frequency of transfusion and QoL; (iii) there is a positive relationship between duration of hospitalization and QoL.

Methods

Participants

This was a cross-sectional design study on adolescent with β-thalassaemia in the state of Kelantan, Terengganu, Pahang, Kedah and Sabah located in Malaysia. Convenient sampling was used to gather the participants from government hospitals when they attend the Day Care Clinic for medical check-up in the period of May 2013 to May 2016. Patients diagnosed with thalassaemia whose age range from 9 to 19 years old and are able to read, understand, and write in Bahasa Malaysia was approached. For participants 18 years old and above, consent was obtained from the patients themselves while consent from patients 17 years old and below was obtained from their caregiver. A total of 218 patients agreed to participate in the research. Once the patients or caregivers have consented to be part of the research, the patients were given a set of self-report questionnaire to be completed. A small token of appreciation was given to all the participants once the self-report questionnaire was completed and returned. Ethical approval for this study was granted by the Human Research Ethics Committee, Universiti Sains Malaysia (FWA Reg. No: 00007718; IRB Reg. No: 00004494) and ethics committee of the Ministry of Health, Malaysia.

Measurements

Socio-demographic and illness related variables were obtained through self-report where participants were asked to fill in their background information in the demographic section of the questionnaire. Some items are open ended such as age, age of diagnosis, and level of education while others are given specific answers to select from such as items related to gender, treatment center, level of education, frequency of hospitalization, and frequency of transfusion.

The Pediatric Quality of Life Inventory 4.0 (PedsQL) was then administered to mainly assess health-related QoL among children and adolescents. Participants were presented with 23 items related to physical, emotional, social, and school functioning for example: "*I feel afraid and scared*" and "*I have trouble getting along with other kids*". Each item has a Likert scale of 0 (never) to 4 (almost always) to be responded by the participants. Scores were transformed into percentage in which high percentage either represents higher functioning, health, or QoL. The validated and reliable Malay translated version of the PedsQL [16] was used in this study. The reliability of the tool in this research was found to be within the acceptable range (Cronbach alpha = .87)

Results

Socio-demographic and illness-related information

The socio-demographic and illness related information are summarized in Table 1. A total of 218 patients with the age ranging from 9 to 19 years old (Mean = 13.86, SD = 2.40) participated in the research in which

107 (48.64%) are males and 113 (51.36%) are females. The age of diagnosis ranges from a few month after birth to 16 years old with the mean of 3.00 and a standard deviation of 3.18. A total of 47 (21.4%) participants were from Kelantan, 32 (14.5%) from Terengganu, and 40 (18.2%) from Pahang; representing he East Coast of

Peninsular Malaysia while 36 (16.4%) patients were from Kedah representing the Northern of Peninsular Malaysia, and 65 (29.5%) from Sabah in East Malaysia. The patients' level of education ranges from not schooling to college or equivalent to college in which 74 (33.6%) participants are currently attending primary school while

113 (60.5%) are attending secondary school. The majority of the participants are hospitalized at least once a month (45.5%) with only two participants hospitalized once to three time a year (0.9%). The most common frequency of transfusion is once every month which applies to 134 (60.9%) participants.

Table 1. Socio-demographic and illness-related characteristics of participants

	Adolescents with β-Thalassaemia (n = 218)	
	Mean (SD)	Range
Age	13.86 (2.40)	9 – 19 years old
Age diagnosed	3.00 (3.18)	<1 – 16 years old
Gender	n (%)	
• Male	108 (48.6)	
• Female	112 (51.4)	
Centre of treatment		
• Kelantan	47 (21.6)	
• Terengganu	32 (14.7)	
• Pahang	39 (17.9)	
• Kedah	35 (16.1)	
• Sabah	65 (29.8)	
Recent educational level		
• Not schooling	1 (0.5)	
• Primary 1	8 (3.7)	
• Primary 2	64 (29.4)	
• Secondary 1	93 (42.7)	
• Secondary 2	40 (18.3)	
• College or equivalent	12 (5.5)	
Frequency of hospitalization		
• 1-3 times a year	2 (0.9)	
• Once every 4 months	4 (1.8)	
• Once every 3 months	21 (9.6)	
• Once every 2 months	48 (22.0)	
• Once every month	99 (45.4)	
• Once every 2-3 weeks	9 (4.1)	

Frequency of transfusion	
• Once every 3 months	2 (0.9)
• Once every 2 months	50 (22.9)
• Once every month	133 (61.0)
• Once every 3 weeks	23 (10.6)
• Once every 2 weeks	10 (4.6)

QoL scores

The mean scores of the four PedsQL subscales and the Psychosocial Health Summary can be seen in Table 2. In addition to the findings from the current study, findings from previous studies using similar outcome measure from different regions are presented to provide a purposeful comparison. The participants in this study was found to have higher total summary score (Mean = 69.64, SD = 14.03), psychosocial health (Mean = 70.23, SD = 14.91), emotional (Mean = 72.12, SD = 20.66), social (Mean = 79.82, SD = 17.37), and school (Mean = 58.69, SD = 16.77) functioning as compared to previous study done in Kuala Lumpur, Malaysia [5]. However, the physical health (Mean = 68.50, SD = 17.22) was found to be lower than the previous study [5]. A detailed comparison can be seen in Table 2.

Table 2. QoL scores based on PedsQL of adolescents with thalassaemia of current and previous studies

Authors (Year)	Location	Patients with thalassaemia (N) Age range (years) Age (Mean; SD)	Total Summary Score	Physical Health	Psychosocial Health	Emotional Functioning	Social Functioning	School Functioning
			Mean (SD)					
Current findings (2017)	Multi-centre (Kelantan, Pahang, Terengganu, Kedah, Sabah), Malaysia	218 9 – 19	69.64 (14.03)	68.50 (17.22)	70.23 (14.91)	72.12 (20.66)	79.86 (17.37)	58.69 (16.77)
Ismail et al. (2013)	Kuala Lumpur, Malaysia	75 5 – 18 (12.1; 3.5)	65.35 (10.57)	69.67 (12.51)	63.91 (14.65)	59.92 (16.83)	78.01 (13.92)	50.59 (15.31)
Boonchooduang et al. (2015)	Chiang Mai, Thailand	64 13 – 18 (15.18; 1.72)	76.10 (12.69)	77.27 (14.96)	75.80 (12.86)	74.02 (17.26)	85.81 (14.08)	67.58 (17.30)
Elalfy et al. (2016)	Ain Shams, Egypt	127 5 – 18 (11.80; 4.78)	63.74 (13.2)	58.46 (18.09)	Not reported	68.22 (13.88)	67.48 (19.31)	63.15 (19.31)
Gupta & Jindal (2016)	Northern India	50 2 – 18 (Not reported)	Not reported	71.40 (33.5)	67.80 (32.9)	66.50 (33.9)	75.50 (36.9)	60.40 (35.4)
Shakib et al. (2016)	Northern Iran	45 8 – 12 (Not reported)	75.90 (20.1)	70.60 (24)	77.70 (19.7)	73.30 (22.9)	85.90 (21)	74.10 (20.1)

Relationship between socio-demographic and illness related variables, and QoL

The associations between the variables of interest were obtained through Pearson product-moment correlation (see Table 3). There is a significant positive correlation between age and age of being diagnosed ($r = .223$, $p < 0.01$), level of education ($r = .824$, $p < 0.01$), frequency of transfusion ($r = .161$, $p < 0.05$), physical health ($r = .210$, $P < 0.01$), and QoL ($r = .155$, $p < 0.05$). In addition, age the patient was diagnosed was found to be significantly correlated with level of education ($r = .238$, $p < 0.01$). Findings also shows a significant positive correlation between level of education and frequency of hospitalization ($r = .156$, $p < 0.05$), frequency of transfusion ($r = .152$, $p < 0.05$), and physical health ($r = .186$, $p < 0.01$). An increase in frequency of transfusion was found to significantly increase social functioning ($r = .137$, $p < 0.05$).

Table 3. Pearson product-moment correlations between socio-demographic and illness related variables with the QoL of adolescents with thalassaemia

	VARIABLES	MEAN (SD)	1	2	3	4	5	6	7	8	9	10
1	Age	13.86 (2.40)										
2	Age diagnosed	3.00 (3.18)	**.223****									
3	Education	2.91 (.94)	**.824****	**.238****								
4	Freqency of hospitalization	3.45 (.92)	.055	.140	**.156***							
5	Frequency of transfusion	2.95 (.75)	**.161***	.043	**.152***	.036						
	Pediatric Quality of Life (PedsQL)											
6	Physical	68.50 (17.22)	**.210****	.082	**.186****	-.016	.047					
7	Emotional	72.12 (20.66)	.076	.094	.086	.052	.020	**.424****				
8	Social	79.86 (17.37)	.116	.071	.081	.029	**.137***	**.508****	**.586****			
9	School	58.69 (16.77)	.033	.135	.002	-.043	.089	**.473****	**.471****	**.426****		
10	Psychosocial health	70.23 (14.91)	.093	.124	.072	.018	.094	**.570****	**.865****	**.818****	**.757****	
11	Total Summary Score	69.64 (14.03)	**.155***	.123	.130	.005	.087	**.822****	**.781****	**.783****	**.727****	**.937****

*p<.05
**p<.01

Discussion

The objective of this study was to examine the relationship between socio-demographic and disease-related variable with the QoL among adolescents with β-thalassaemia in multiple treatment centers in Malaysia. As a group, adolescents with β-thalassaemia in this multi-center study were found to have a slightly higher emotional and social functioning as compared to their counterparts in Kuala Lumpur – the capital city of Malaysia [5]. However, the school functioning and physical health was found to be slightly lower while their psychosocial health and total summary score of the participants in this research was found to be slightly higher than the participants in the previous study done in Kuala Lumpur [5]. When compared to studies carried out in Thailand [6] and Northern Iran [17], participants in the current study were found to have slightly lower scores in all domains of PedsQL including the total summary score and psychosocial health. However, only the psychosocial health, emotional functioning and social functioning of adolescents with thalassaemia in Malaysia is slightly higher when compared to individuals with thalassaemia in Northern India [10]. The physical health and school functioning of individuals with thalassaemia in Northern India was found to be higher than that of Malaysian [10]. Although these differences may not be statistically significant, it provides an understanding of the QoL among adolescents with thalassaemia with respect to the different socio-economic development and the illness related variable of each region.

The positive association between age and education level is expected as thalassaemia symptoms do not hinder them from attending school. Although their education level is appropriate for their chronological age, the scores for their school functioning is the lowest compared to their emotional and social functioning. This is similar to numerous studies in the past, in which adolescents with thalassaemia is able to obtain equivalent academic exposure but is not present in school as frequent as their peers due to treatment [5, 6, 10]. However, in some regions, the school functioning is not the most effected functioning since treatment related to transfusion is done on weekends [11, 17]. This suggests that adolescents with thalassaemia has the capability to function well in school but is hindered due to the treatment that requires them to be absent from school. This is where the understanding of health policies in different countries and its implication to the QoL of adolescents with thalassaemia is helpful in providing optimal care for them.

Additionally, the frequency of performing transfusion was found to increase significantly as the age of the patient increases, which is consistent with findings from previous studies [18, 19]. This could be due to the increase in blood volumes [18] and the increase in severity of the symptoms as they grow older [19]. The increased in the frequency of transfusion could also be reflected from the treatment adherence which could be explained from the developmental perspective. Taddeo *et al.* [20] considered developmental stages as one of the critical factors when discussing treatment adherence. As an individual age increases and their cognitive development transitions from a concrete thinking to a more abstract thinking, they are able to think more hypothetically and analyze many different evidences that help them appreciate the treatment process. Treatment adherence can be improved by taking into consideration the child's cognitive

development and providing appropriate information clearly and concisely using short and simple sentences [20]. This explains how adolescents with thalassaemia who may have transitioned from concrete thinking to a more abstract thinking are able to critically assess the importance of the transfusion with information provided by the medical providers, leading to an increased in transfusion for older participants. The finding that an increase in education level significantly increased frequency of transfusion could also support this view.

The physical health and QoL of adolescent with thalassaemia increases as they grow older contradicts previous studies that found significant growth retardation as compared to healthy group [21, 22]. However, patients with thalassaemia are physically stable and fit so much so that they are capable of performing near-normal physical activity similar to the healthy population [23, 24]. This means that even though the physical growth of adolescent with thalassaemia is delayed as compared to healthy population; they are able to perform physical activity that is appropriate to their growth, with them experiencing a slight difficulty in performing activities of daily living independently. This also applies to their QoL that gets better as their age increases [23]. Additionally, the advancement of medication ensures that the growth retardation does not influence the functioning of adolescents with thalassaemia [25]. This is reflected in the findings in this study that showed an increase in frequency of transfusion significantly increased their social functioning.

Conclusion

The QoL of adolescents with thalassaemia for states in the East, North and East Coast of Malaysia was found to be slightly higher than the patients with thalassaemia in Kuala Lumpur. However, there are still rooms for improvements as the QoL of adolescents with thalassaemia in Malaysia is found to be lower than that of other regions such as Thailand and Northern Iran. There is a need to study the cross cultural differences that exist in the health policies or socio-demographic and illness related variables to ensure a universal optimal care for adolescents with thalassaemia regardless of the region they are in.

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References

[1] Rund D, Rachmilewitz E. Medical progress : β -Thalasemia. The New England Journal of Medicine. 2005;353:1135-1146.

[2] Sayani FA, Kwiatkowski JL. Increasing prevalence of thalassaemia in America: Implications for primary care. Annals of Medicine. 2015;47(7):592–604.

[3] Finotti A, Breda L, Lederer CW, Bianchi N, Zuccato C, Kleanthous

M, et al. Recent trends in the gene therapy of β -thalassaemia. Journal of Blood Medicine. 2015;6:69–85.

[4] Telfer P, Constantinidou G, Andreou P, Christou S, Modell B, Angastiniotis M. Quality of life in thalassaemia. Annals of the New York Academy of Sciences. 2005;1054:273-82.

[5] Ismail M, Chun CY, Shahar S, Manaf ZA, Rajikan R, Mohd Yusoff NA, et al. Quality of life among thalassaemia children, adolescent and their caregivers. Sains Malaysiana. 2013;42(3):373–380.

[6] Boonchooduang N, Louthrenoo O, Choeyprasert W, Charoenkwan P. Health-Related Quality of Life in Adolescents with Thalassaemia. Pediatric Hematology and Oncology. 2015;32(5):341–348.

[7] Shah AA, Othman A. Hospitalization, later onset of the disease, and psychological problems of chronically ill children. SAGE Open. 2013;3(4):1-10.

[8] Surapolchai P, Satayasai W, Sinlapamongkolkul P, Udomsubpayakul U. Biopsychosocial predictors of health-related quality of life in children with thalassaemia in Thammasat University Hospital**.** Journal of Medical Association Thailand. 2010;7:65-75.

[9] Tsiantis J, Dragonas T, Richardson C, Anastasopoulos D, Masera G, Spinetta J. Psychosocial problems and adjustment of children with beta-thalassaemia and their families. European Child & Adolescent Psychiatry. 1996;5(4):193–203.

[10] Gupta M, Jindal, R. Quality of life in patients with thalassaemia major. International Journal of Science and Research. 2016;5(5):41-42.

[11] Elalfy MS, Farid MN, Labib JH, RezkAllah HK. Quality of life of Egyptian beta-thalassaemia major children and adolescents. Egyptian Journal of Haematology. 2017;39(4):222-226.

[12] Coacci G, Efficace F, Ciotti F, Roncarolo MG, Vacca A, Piras E, et al. Health related quality of life in Middle Eastern children with beta-thalassaemia. BMC Blood Disorders. 2012;12(6):1-7.

[13] Abetz L, Baladi J, Jones P, Rofail D. The impact of iron overload and its treatment on quality of life: results from a literature review. Health and Quality of Life Outcomes. 2006;4:73.

[14] Porter J, Bowden DK, Economou M, Troncy J, Ganser A, Habr D, et al. Health-related quality of life, treatment satisfaction, adherence and persistence in β -thalassaemia and myelodysplastic syndrome patients with iron overload receiving deferasirox: Results from the EPIC clinical trial. Anemia. 2012 Aug 12:1-10.

[15] Scalone L, Mantovani LG, Krol M, Rofail D, Ravera S, Bisconte MG, et al. Costs, quality of life, treatment satisfaction and compliance in

patients with beta-thalassaemia major undergoing iron chelation therapy: the ITHACA study. Current Medical Research and Opinion. 2008;24(7):1905–1917.

[16] Kaartina S, Chin YS, Wahida RF, Woon FC, Hiew CC, Zalilah MS, Nasir MTM. Adolescent self-report and parent proxy-report of health-related quality of life: an analysis of validity and reliability of PedsQL™ 4.0 among a sample of Malaysian adolescents and their parents. Health and Quality of Life Outcomes. 2005;13:44-52.

[17] Jafari-Shakib A, Davoudi-Kiakalaye A, Pour-Fathollah AA, Jafari-Shakib R, Mohtasham-Amiri Z. Health-related quality of life in β - thalassaemia major children in North of Iran. Iranian Journal of Blood and Cancer. 2016;8(4):108–111.

[18] Davies P, Robertson S, Hegde S, Greenwood R, Massey E, Davis P. Calculating the required transfusion volume in children. Transfusion. 2007:47(2):212–216.

[19] Shah N, Mishra A, Chauhan D, Vora C, Shah N R. Study on effectiveness of transfusion program in thalassaemia major patients receiving multiple blood transfusions at a transfusion centre in Western India. Asian Journal of Transfusion Science. 2010;4(2):94–98.

[20] Taddeo D, Egedy M, Frappier JY. Adherence to treatment in adolescents. Paediatrics & Child Health. 2008;13(1):19–24.

[21] George A, Bhaduri A, Sen S, Choudhry VP. Physical growth parameters in thalassemic children. Indian Journal of Pediatrics. 1997:64(6):861–71.

[22] Gomber S, Dewan P. Physical growth patterns and dental caries in Thalassaemia. Indian Pediatric. 2006;43(12):1064–1069.

[23] Angastiniotia M. Lifestyle and quality of life. In: Cappellini MD, Cohen A, Porter J, Taher J, Viprakasit V, editors, Guidelines for the management of transfusion dependent thalassaemia Nicosia, Cyprus: Thalassaemia International Federation: 2014. p. 224-235.

[24] Galanello R, Origa R. Beta-thalassaemia. Orphanet Journal of Rare Diseases. 2010;5:1–15.

[25] Yamashita R, Mednick L, Haines D. Psychological support. In: Cappellini MD, Cohen A, Porter J, Taher A, Viprakasit V, editors. Guidelines for the management of transfusion dependent thalassaemia. Nicosia, Cyprus: Thalassaemia International Federation: 2014. p. 224-235.