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Quality of Life Among Thalassaemia Children, Adolescent and Their Caregivers

(Kualiti Hidup Pesakit Talasemia Kanak-Kanak dan Remaja serta Penjaga Mereka)

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ABSTRACT

In thalassaemic patients, the impact of the disease especially on quality of life (QOL) of the caregivers in Malaysia has not been established. This study was conducted to assess the health-related quality of life (HRQOL) of thalassaemia patients and their caregivers in order to explore factors affecting their QOL. A cross-sectional study was conducted on 75 thalassaemic children and adolescents aged between 7 and 18 years old and their caregivers. The PedsQL™ 4.0 generic core scales questionnaire was administered to both thalassaemic children and their caregivers while the health questionnaire EQ 5D was given to caregivers only. The subjects were recruited from Hospital Kuala Lumpur (HKL) and Universiti Kebangsaan Malaysia Medical Centre (UKMMC). The results revealed that the mean of psychosocial HRQOL score in patients (63.91±14.65) was significantly lower than parent proxy reports (67.14±10.48) (p=0.008). The school functioning score (50.59±15.31) was the lowest of the psychosocial measure, followed by emotional functioning (59.92±16.83) and social functioning (78.01±13.92) score. The patients' pre-transfusion haemoglobin concentration was significantly associated with their QOL (p=0.02). Having more children, higher numbers of thalassaemic children and lower educational level of caregivers were associated with poorer QOL. In conclusion, caregivers underestimated the QOL of their thalassaemic children. The school functioning domain was affected the most domain. There is a need to improve the QOL of thalassaemic children and their caregivers.

Keywords: Caregivers; education; paediatrics; quality of life; thalassemia

ABSTRAK

Bagi pesakit talasemia, kesan penyakit terutamanya ke atas kualiti hidup penjaga mereka di Malaysia masih belum difahami. Penyelidikan ini telah dijalankan untuk menilai kualiti hidup berkaitan kesihatan (HRQOL) dalam kalangan pesakit talasemia serta penjaga mereka bagi mengetahui faktor-faktor yang mempengaruhi kualiti hidup mereka. Kajian keratan lintang telah dijalankan ke atas 75 pesakit talasemia kanak-kanak dan remaja berumur antara 7 dan 18 tahun serta penjaga mereka. Borang soal-selidik PedsQL™ 4.0 generic core scales telah diberikan kepada pesakit dan penjaga sementara borang soal-selidik kesihatan EQ 5D diberikan kepada penjaga sahaja. Subjek direkrut dari Hospital Kuala Lumpur (HKL) dan Pusat Perubatan Universiti Kebangsaan Malaysia (PPUKM). Keputusan menunjukkan min skor HRQOL psikososial dalam kalangan pesakit (63.91±14.65) adalah lebih rendah secara signifikan berbanding laporan proksi penjaga (67.14±10.48) (p=0.008). Skor fungsian sekolah (50.59±15.31) adalah paling rendah antara pengukuran psikososial, diikuti skor fungsian emosi (59.92±16.83) dan fungsian sosial (78.01±13.92). Kepekatan hemoglobin pra-transfusi berkait secara signifikan dengan kualiti hidup mereka (p=0.02). Anak yang lebih ramai, jumlah anak yang menghidap talasemia yang lebih ramai serta tahap pendidikan penjaga yang rendah dikaitkan dengan kualiti hidup yang kurang memuaskan. Kesimpulannya, penjaga didapati memandang rendah isu kualiti hidup anak-anak talasemia mereka. Domain fungsian sekolah didapati paling bermasalah. Oleh itu, terdapat keperluan untuk meningkatkan kualiti hidup pesakit talasemia kanak-kanak dan remaja serta penjaga mereka.

Kata kunci: Kualiti hidup; pediatrik; pendidikan; penjaga; talasemia

INTRODUCTION

Thalassaemia indicates a heterogeneous group of genetic disorders of haemoglobin synthesis characterized by a disturbance of globin chains' production, leading to anaemia, ineffective erythropoiesis and destruction of erythroblast in the bone marrow and erythrocytes in the peripheral blood (Higgs et al. 2001). Alpha thalassaemia is commonly found in southern Asia and southern China. However, beta thalassaemia is more common in the Mediterranean countries, the Middle East, the Indian subcontinent, South East Asia, Russia and northern China (Leung et al. 2008; Olivieri & Brittenham 1997; Weatherall 1981). The ethnic population of Malaysia comprises Malays (54.3%), Chinese (25%), Indians (7.5%) and other indigenous group (13.2%) (Department of Statistic Malaysia 2010). In Malaysia, thalassaemia occurs mainly amongst the Malays and Chinese population. Approximately 4.5% of Malaysians are heterozygous

carriers of beta thalassaemia and these couples are at risk of having a child with beta thalassaemia major; affected annual births is estimated to be 2.1/1,000 (George 2001). The Malaysian Ministry of Health estimated that about 150 to 350 babies are born each year with thalassaemia (Tam 2005). George (2001) estimated that there were 5,600 blood transfusion dependent beta thalassaemia patients in Malaysia.

Thalassaemia affects patients' health-related quality of life (HRQOL). Children with thalassaemia major have to undergo blood transfusion at least once a month, depending on the severity of the disease. Iron chelation therapy such as desferrioxamine is required to remove excessive iron in the blood, which resulted from regular blood transfusion (Anionwu & Atkin 2001; Saeed 2004). In addition, the disease itself may have profound impact on the patients' physical appearance, such as bone deformities and short stature which leads to poor self-image (Ismail et al. 2006; Telfer et al. 2005).

The paediatric health-related quality of life (HRQOL) measurement is recognized as an important health outcome in the trial, review and evaluation of health services (Matza et al. 2004; Varni et al. 1999). Although efforts to measure quality of life (QOL) of children are complex, more and more generic measures of disease-specific tools have been reported (Eiser & Morse 2001). HRQOL of the physical, psychological and social domains of health are influenced by experiences, beliefs, expectations and perceptions (Matza et al. 2004). HRQOL is a multidimensional concept that represents the patient's overall perception regarding the impact of the illness and its treatment (Shumaker & Berzon 1995). It can be used to describe the impacts of the disease or illness in individuals in addition to evaluating the impact of individual treatments or programs of services to the population. Furthermore, assessment of HRQOL can also predict the future status of people with a certain illness (Spilker 1996).

As there are limited studies focusing on thalassaemic children and their caregivers QOL, the aim of this study was to assess the health-related quality of life (HRQOL) of thalassaemia children, adolescents and their caregivers in order to explore factors affecting their quality of life to improve overall management.

Materials and Methods

A cross-sectional study was conducted among children and adolescents, aged 7 and 18 years old with beta thalassaemia major, HbE beta thalassaemia and thalassaemia intermedia who received regular blood transfusion treatment (1 to 3 times monthly) at Hospital Kuala Lumpur (HKL) and Universiti Kebangsaan Malaysia Medical Centre (UKMMC) and their caregivers, from August 2009 till January 2010. The study was approved by the National Institute of Health (NIH) (NMRR-09-289-3405) and Ethics Committee, Medical Research Secretariat, UKMMC (FF-290-2008). In addition to age, further inclusion criteria for patients were ability to read, write and understand Malay, English or Mandarin. The caregivers were defined as either the father or mother of the patient. Written informed consent was obtained from all participants.

The quality of life assessment of patients was performed using the paediatric quality of life inventory™ (PedsQL™) 4.0 generic core scale which was developed to measure health-related quality of life (HRQOL) in healthy children and adolescent and those with acute and chronic health problems. A user agreement was signed with the MAPI Research Institute, Lyon, France, prior to the use of the questionnaire. The PedsQL 4.0 generic core scale was designed for developmentally appropriate which includes parallel child self reports and parent proxy reports (age ranges 5-7, 8-12 and 13-18 years) were administered following the PedsQL™ administration guidelines℠. PedsQL items required subjects to report problems regarding physical, emotional, social and schooling function that have arisen for the past one month. The 23 items' responses were measured on a five-point rating scale ranging from 0 (never a problem) to 4 (almost always a problem), yielding a total score and two summary scores (i.e. physical health and psychosocial health). Each scale had a score ranging from 0 to 100, the higher score indicating higher QOL. The PedsQL has demonstrated good internal consistency and validity in large samples of children with acute and chronic health conditions, as well as in healthy children and adolescents. Furthermore, its reliability has been tested by the previous use of the PedsQL 4.0 generic core scale (Malay version) in Malaysia (Ismail et al. 2006).

The quality of life assessment of patients' caregivers was performed using EQ 5D descriptive system which consists of five dimensions as follows: mobility, self care, usual activity, pain/discomfort and worry/depression. Each dimension had three levels: no problems, some problems and severe problems. The respondents were asked to indicate his/her health state by ticking in the box against the most appropriate statement in each of the five dimensions. This decision resulted in a 1-digit number expressing the level selected for that dimension. The digits for five dimensions were combined in a 5-digit number describing the respondent's health state. Validation was done and reliability for use in Malaysia has been tested (Mahadeva et al. 2008; van Agt et al. 1994).

Socio demographic data and clinical parameters were obtained from the patients' medical records. These included demographics of the patients (gender, age, ethnic and educational level) and clinical information (type of thalassaemia, onset of thalassaemia, haemoglobin (Hb) level, type of chelation therapy, age at first transfusion frequency of blood transfusion and iron chelation treatment).

Statistical analysis was carried out using statistical package for social sciences (SPSS) version 16. General characteristics of the patients were presented in terms of percentage, mean and standard deviation. Differences in the health-related quality of life (HRQOL) score between thalassaemia patients' self report and parent's proxy report were tested using the Mann-Whitney test. For HRQOL, both

total HRQOL score and summary scores were presented in terms of mean and standard deviation. Mann-Whitney U, Kruskal-Wallis and the chi-square test were used to examine the relationship between HRQOL and each demographic/clinical parameter. A p value of ≤0.05 was considered statistically significant.

Results and Discussion

A total of 75 thalassaemic patients from Hospital Kuala Lumpur (HKL) and UKM Medical Centre (UKMMC) and 64 caregivers were approached. The majority of patients were Malays (69%), followed by Chinese (25%) and other ethnic groups (5%) (Table 1). The mean age of patients was 11.9±3.3 years for boys and 12.3±2.8 for girls. The majority of patients (44%) are from families with household incomes of RM1500-RM3000 (USD484.97-USD969.93). The percentages of patients diagnosed with beta-thalassaemia major, HbE-beta thalassaemia and thalassaemia intermedia were 72%, 23% and 5%, respectively. The mean duration of diagnosis is 9.93 ± 3.40 years with mean duration of chelation therapy is 8.69 ± 4.19 years. The mean pre-transfusion haemoglobin concentration measured three months prior to the HRQOL assessment was approximately 8.88±1.69 g/dL. The majority of patients received blood transfusion once per month (88%) and chelation treatment 3 to 6 times per week (56%). Sixty-three percent of the caregivers were mothers. The mean age of caregivers was 45.3±6.3 years for men and 42.9±6.6 years for women. The majority of caregivers hailed from high educational background (upper secondary and above) (73%), were from the urban area (63%) and were working (58%). The majority of caregivers also had 1 to 3 children (67%) and most of them had only one child with thalassaemia (69%).

TABLE 1. Demographic and clinical characteristics of thalassaemia patients

	Mean ± SD	*n* (%)
Gender (*n*=75)		
Female		36 (48)
Male		39 (52)
Age (years)(*n*=75)		
5 – 7		6 (8)
8 – 12		34 (45)
13 – 18		35 (47)
Educational level (*n*=75)		
No formal education		1 (1)
Primary school		41 (55)
Lower secondary school		27 (36)
Higher secondary school and above		6 (8)
Family income (*n*=68)	RM3206.3 ± 2852.7 USD1036.6 ± 922.3	
< RM1500 (USD 484.97)		15 (20)
RM1500-RM3000 (USD484.97-969.93)		30 (40)
> RM3000 (USD969.93)		23 (30)
Hb (*n*=57)	8.88 ± 1.69	
< 7 g/dL		6 (11)
7-9 g/dL		24 (42)
> 9 g/dL		27 (47)
Type of chelation (*n*=73)		
None		8 (11)
Desferrioxamine		51 (70)
Deferasirox		13 (18)
Deferiprone		1 (1)
Frequency of transfusion (*n*=75)		
4-6 monthy		1 (1)
2-3 monthly		8 (11)
Monthly		66 (88)
Frequency of chelation therapy (*n*=72)		
None		8 (11)
Daily		21 (29)
3-6 times per week		40 (56)
<3 times per week		3 (4)

*RM is an acronym for Malaysian Ringgit

In this study, we found that the mean total summary scores among thalassaemia children (65.35±10.57) were lower than parents' proxy reports (67.20±11.36); *p* value was however 0.136 (Table 2), while physical functioning score for patients' self report (69.67±12.51) was higher than the parents' proxy report (67.25±14.28), but with *p* value 0.337. The mean psychosocial health score was significantly lower ($p<0.01$) for patients' self report (63.91±14.65) than for parents' proxy report (67.14±10.48). Psychosocial subscale revealed that school functioning scored the lowest for both patients' self report (50.59±15.31) and parents' proxy report (52.21±18.85) ($p=0.605$). These findings are consistent with previous studies that showed parents may overestimate or underestimate patients' QOL while some studies showed high correlation between both reports. (Baraz et al. 2010; Eiser & Morse 2001; Matza et al. 2004; Reinfjell et al. 2006; Russell et al. 2006; Simeoni et al. 2001; Varni et al. 2006). The mean total summary score of patients' self report in this study was lower compared with findings by Ismail et al. (2006) which was 68.91±12.12. On the other hand, mean physical functioning score and mean social functioning score of patient's self report in this study was higher compared with Ismail et al. (2006) which were 69.15±16.45) and 74.29±18.77, respectively. Ismail et al. (2006) had conducted a study to evaluate the HRQOL status of 64 thalassaemia patients in Kuala Lumpur, Malaysia using the PedsQL 4.0.

The mean psychosocial health score of patients' self report (63.91±14.65) in our study was lower compared with Ismail et al. (2006) which was 67.58±12.77. This low psychosocial health score supports previous studies on patients with thalassaemia, whereby more psychosocial support should be given to thalassaemia patients not only from the government but also from non-government organisations such as the Thalassaemia Association of Malaysia (Aydinok et al. 2005; Goldbeck et al. 2000).

In our study, the score for emotional functioning subscale was lower compared with previous studies. Mean emotional function score was reported to be 68.14±17.22 by Ismail et al. (2006) while a study by Upton et al. (2005) on children had reported that mean emotional function score for children with athme, cancer and diabetes was 70.66±20.06, 73.56±18.39 and 78.85±18.28, respectively. According to Pakbaz et al. (2005) emotional functioning is one of the weaker domains among thalassaemia children as they experience anxiety, depression and concerns over their health status. As with previous studies, the school functioning subscale scored the lowest (Ismail et al. 2006). This low school functioning score is due to patients requiring regular blood transfusion in hospital; as a result patients are intermittently absent from school which ultimately gave a negative impact on their HRQOL (Anionwu & Atkin 2001; Saeed 2004).

Pre-transfusion haemoglobin (Hb) level, frequency of transfusion and frequency of chelation therapy were found to be significant predictors of HRQOL scores (Tables 3 & 4). The study revealed that patients whose Hb level was higher than 9 g/dL had a significantly higher ($p=0.02$) total summary score (68.41±7.69) than those with Hb levels of 7-9 g/dL (66.00±8.98) or less than 7 g/dL (46.30±17.53) in patients' self report. This result is supported by Dahlui et al. (2009) in his study on thalassaemia patients and also consistent with the findings from several studies conducted on other diseases that also address the association between Hb concentration and quality of life (Afsar et al. 2009; Finkelstein et al. 2008; Santos 2008; Thein et al. 2009). Lower Hb level is associated with a number of symptoms, such as fatigue, general weakness and decreased mental alertness, which may lead to impaired HRQOL of the patients (Shumaker & Berzon 1995). Pre-transfusion Hb level should be monitored routinely to maintain an optimal level of 9-10.5 g/dL (Shaligram et al. 2007).

As reported in previous studies, we found that there was a significant relationship between frequency of blood transfusion and HRQOL ($p=0.034$), with patients receiving more frequent blood transfusion having lower psychosocial health score when compared with patients receiving less frequent blood transfusion (Anionwu & Atkin 2001; Saeed 2004). The patients typically have to undergo for blood transfusions at least once a month depending on the severity of the illness. This means attendance for an entire day at the hospital which leads to school absenteeism and might impaired HRQOL indirectly. Our study also showed that frequency of iron chelation treatment was significantly related to HRQOL impairment

TABLE 2. Comparison of PedsQLTM 4.0 score between patients' self report and parents' proxy report

Scale	Patients' self report (*n*=75) Mean ± SD	Parents' proxy report (*n*=75) Mean ± SD	*p* value
Total summary score	65.35 ± 10.57	67.20 ± 11.36	0.136
Physical functioning	69.67 ± 12.51	67.25 ± 14.28	0.337
Psychosocial health	63.91 ± 14.65	67.14 ± 10.48	0.008
Emotional functioning	59.92 ± 16.83	74.06 ± 5.36	0.000
Social functioning	78.01 ± 13.92	76.03 ± 3.73	0.027
School functioning	50.59 ± 15.31	52.21 ± 18.85	0.605

Mann Whitney Test

TABLE 3. Patients' self report HRQOL score based on clinical characteristics

Mean ± SD	Total summary	Physical functioning	Psychosocial health
Hb			
< 7 g/dL (*n*=6)	46.30 ± 17.53	51.04 ± 14.34	44.72 ± 19.02
7-9 g/dL (*n*=24)	66.00 ± 8.98	69.92 ± 9.43	64.69 ± 11.07
> 9g/dL (*n*=27)	68.41 ± 7.69	73.73 ± 13.29	66.64 ± 8.03
p value[a]	0.020	0.008	0.021
Frequency of transfusion			
4-6 monthly (*n*=1)	90.47	71.88	96.67
2-3 monthly (*n*=8)	72.29 ± 9.36	66.02 ± 7.36	74.38 ± 11.82
Monthly (*n*=66)	64.02 ± 10.24	69.91 ± 13.38	62.06 ± 10.48
p value[a]	0.072	0.733	0.034
Frequency of chelation therapy			
None (*n*=8)	71.41 ± 10.56	69.14 ± 5.89	72.17 ± 13.22
Daily (*n*=21)	66.05 ± 11.10	70.94 ± 12.79	64.70 ± 12.34
3-6 times a week (*n*=40)	65.52 ± 8.47	70.09 ± 13.03	63.71 ± 8.88
<3 times a week (*n*=3)	48.91 ± 10.13	57.29 ± 6.51	46.11 ± 11.34
p value[a]	0.036	0.140	0.031

Kruskal-Wallis Test

TABLE 4. Parents' proxy report HRQOL score based on clinical characteristics

	Mean ± SD		
	Total summary	Physical functioning	Psychosocial health
Hb			
< 7 g/dL (*n*=6)	72.19 ± 10.70	71.88 ± 13.83	72.50 ± 10.21
7-9 g/dL (*n*=24)	62.38 ± 11.73	61.47 ± 14.07	63.29 ± 11.15
> 9g/dL (*n*=27)	68.77 ± 9.48	69.59 ± 13.17	67.96 ± 7.84
p value[a]	0.159	0.351	0.176
Frequency of transfusion			
4-6 monthly (*n*=1)	82.50	75.00	90.00
2-3 monthly (*n*=8)	67.82 ± 10.72	67.10 ± 14.61	68.54 ± 10.63
Monthly (*n*=66)	66.66 ± 11.14	66.97 ± 13.70	66.34 ± 10.31
p value[a]	0.485	0.540	0.261
Frequency of chelation therapy			
None (*n*=8)	72.10 ± 8.04	74.61 ± 10.75	69.58 ± 7.33
Daily (*n*=21)	70.17 ± 13.65	70.51 ± 17.87	69.84 ± 11.41
3-6 times a week (*n*=40)	64.71 ± 9.33	63.69 ± 11.00	65.73 ± 10.01
>3 times a week (*n*=3)	56.39 ± 13.83	58.33 ± 18.31	54.44 ± 10.18
p value[a]	0.036	0.030	0.053

Kruskal-Wallis Test

which was similar to other reported studies (Abetz et al. 2006; Shaligram et al. 2006). Patients receiving more frequent chelation treatment (everyday) had higher total summary score (p=0.036), higher physical functioning score (p=0.140) and higher psychosocial health score (p=0.031) as compared with patients receiving less frequent chelation treatment. A more frequent chelation therapy may lead to increment in iron losses which indirectly influence their quality of life.

Concordant with the findings from previous studies, gender, type of thalassaemia (i.e. beta thalassaemia major, HbE-beta thalassaemia and thalassaemia intermedia) and type of chelation were not related to HRQOL (Dahlui et al. 2009). We also found that ethnicity and family income were not significantly related with HRQOL. Similar findings were reported by Ismail et al. (2006) in a study among thalassaemia patients in Malaysia. Age, educational level and patients' BMI were also not significantly related with HRQOL in this study.

Figure 1 shows the proportion and frequency of EQ 5D according to the various dimension. The majority of caregivers reported no concerns in the various dimension of EQ 5D. A total of 84.4%, 100%, 67.2%, 65.6% and 56.2% caregivers reported no issues in dimension mobility, self care, usual activity, pain/discomfort and worry/depression, respectively.

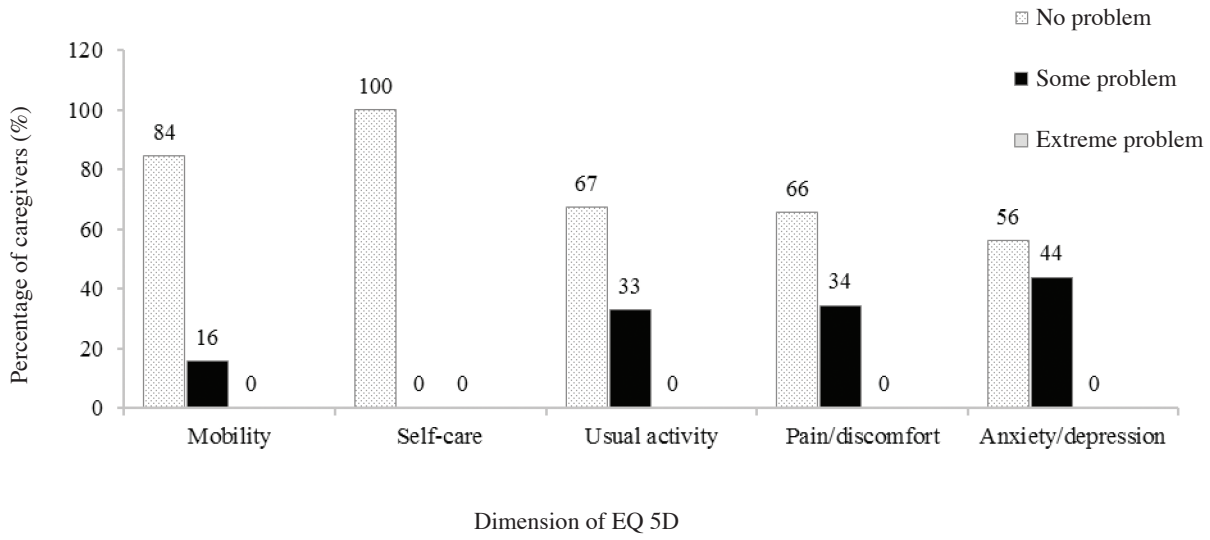

FIGURE 1. Percentage of EQ 5D dimension of caregivers

Caregivers' with more than one thalassaemia child reported more problems with usual activity (p=0.02), pain/discomfort (p=0.25) and anxiety/depression dimensions (p=0.030) (Table 5). It was found that caregivers with lower educational level reported more problems in anxiety/depression dimension when compared with caregivers with higher educational level (p=0.002). Our results showed that caregivers with more than one affected child are faced with more problems. This may be due to increased physical and mental stress resulting in impaired QOL among caregivers. Our findings also found that caregivers with lower educational levels experience more problems. Lower educational level may be associated with poorer understanding of the nature of the disease which in turn may affect the psychosocial aspects of this group of parents.

A limitation of this study was the absence of a control group of healthy children. Nevertheless, the findings of this study highlight the significant negative impact of thalassaemia on patients' HRQOL in terms of physical functioning and psychosocial functioning, especially in the school functioning subscale. The study also found the significant negative impact of thalassaemia on caregivers' HRQOL in terms of various dimensions. Considering that the

TABLE 5. Relationship of various dimensions of EQ 5D with number of children with thalassaemia and caregivers' educational level

Dimension	No of thalassaemia children		p value
	1	>1	
Usual activity			
No problem	34 (79.1)	9 (20.9)	0.020
Some problem	10 (47.6)	11 (52.4)	
Pain/Discomfort			
No problem	33 (78.6)	9 (21.4)	0.025
Some problem	11 (50.0)	11 (50.0)	
Anxiety/Depression			
No problem	29 (80.6)	7 (19.4)	0.030
Some problem	15 (53.6)	13 (46.4)	
	Caregivers' educational level		
	Low (Lower secondary and below)	High (Upper secondary and above)	
Anxiety/depression			
No problem	4 (11.1)	32 (88.9)	0.002
Some problem	13 (46.4)	15 (53.6)	

Chi-square Test
*Values are presented as number (percentage)

prevalence of thalassaemia in Malaysia, our study suggests that improvement of the welfare and social support system should be further improved. Health campaigns can be held to help patients and caregivers cope better with thalassaemia. Patients, school officials, family and hospital officials should always maintain contact and surveillance of their patients' well-being.

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