# Biopsychosocial Predictors of Health-Related Quality of Life in Children with Thalassemia in Thammasat University Hospital

Pacharapan Surapolchai MD*, Wallee Satayasai MD*,
Phakatip Sinlapamongkolkul MD*, Umaporn Udomsubpayakul Bsc**

** Department of Pediatrics, Faculty of Medicine, Thammasat University, Pathumthani, Thailand*
*** Research Center, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand*

***Objectives:*** *To determine health-related quality of life (HRQOL) in children with thalassemia in order to explore physical and psychosocial factors affecting on their QOL.*
***Material and Method:*** *A cross-sectional study was conducted at Thammasat University Hospital, Pathum Thani. Socio-demographic factors and clinical characteristics were obtained from seventy-five of transfusion-dependent and non-transfused thalassemia patients. The PedsQL™ 4.0 Generic Core Scales (Thai version) were administered to determine the patients and their parents' perspectives.*
***Results:*** *The mean (SD) of total HRQOL score was 78.50 (2.05) for children who were self-reporting and it was 73.41 (2.22) for parent proxy-report, that were comparable with population norms. The stepwise multiple regression analysis indicated that total HRQOL score of child self-report was negatively predicted by lower family income, early age onset of anemia before 2 years and under covered by Universal Health Coverage Scheme. The negative predictors of total HRQOL score of parent proxy-report were regular transfusion every 1-2 months, while self medical payment was positively predictive.*
***Conclusion:*** *The HRQOL in children with thalassemia was not only determined by disease severity and treatment but also by family financial impacts for caring of children. Health care interventions should be implemented to support in various domains of life.*

***Keywords:*** *Thalassemia, Health-related quality of life, PedsQL™*

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Thalassemia is the heterogenous group of inherited disorders characterized by decreased or absence of globin synthesis. These disorders represent the most common single-gene disease in human and they have a high frequency in the Mediterranean region, Middle East and South-East Asia[1,2]. In Thailand, 30-40 percent of population carries thalassemia genes. At present, there are 630,000 people nationwide with thalassemia, while 12,000 babies are born with it every year[3].

The current combination of transfusion and iron-chelation therapy has dramatically extended the life expectancy of thalassemia patients. Nevertheless, frequent blood transfusions leading to iron overload and its chronic nature have contributed to a new spectrum of complications in children and adolescents suffering from thalassemia. Apart from physical growth and puberty, quality of life is another issue in long-term follow-up of these patients. Health-related quality of life (HRQOL) measurement is a multidimensional concept that represents the patients' perspectives of the impact of illness and treatment on the well-being of an individual[4,5].

According to assess HRQOL in thalassemia patients, most published studies have indicated the negative impact of disease severity and its treatment on HRQOL[6-8]. However, this approach is sometimes limited to predict the HRQOL status because it does not relevant to the psychosocial context of each patient. In addition, a previous study in adult indicated that transfusion-independent thalassemia patients also suffer impairments in their quality of life[9]. Thavorncharoensap et al[10] recently concluded that

***Correspondence to:***
*Surapolchai P, Department of Pediatrics, Faculty of Medicine, Thammasat University, Pathumthani 12120, Thailand.*
*Phone: 0-2926-9514, Fax: 0-2926-9485*
*E-mail: doctorning@hotmail.com*

age and disease severity were significant predictors of child self-report HRQOL among Thai children with thalassemia; while serum ferritin level, frequency of blood transfusion, and gender were not.

As a limited research assignment on the HRQOL of children with thalassemia patients in particular aspects, Objectives of the study were 1) to evaluate the HRQOL in Thai pediatric patients with transfusion-dependent and non-transfused thalassemia disease; and 2) to examine the biopsychosocial predictors of their HRQOL focusing on children and parents' perspective. The utilization of HRQOL measures will assist in capturing patients' perceptions, healthcare needs and preferences for disease outcomes.

## Material and Method

Children with thalassemia aged 2-18 years, attending the Pediatric Hematology Clinic at the Thammasat University Hospital, were recruited on their routine blood transfusions and follow-up in the period from May 2008 to May 2009. Socio-demographic and clinical characteristics of the patients were collected via medical record review and interview. Most of them have been receiving their treatments at our institute since they were diagnosed as thalassemia. Previously, desferrioxamine had been administered for iron chelation therapy. However, since November 2007, six months before this study was conducted, the institute has provided daily 50-75 mg/kg of locally-manufactured oral deferiprone (GPO-L-ONE from Thai Governmental Pharmaceutical Organization) as single agent and in combination with 20-40 mg/kg of subcutaneous infusion of desferrioxamine two to three days per week in pediatric patients with transfusion-dependent thalassemia disease.

The quality of life assessment in the present report was carried out using the Pediatric Quality of Life Inventory™ (PedsQL™ 4.0), developed by Dr. James W Varni[11,12] and validated in Thai for local used. The PedsQL™ 4.0 Generic Core Scales (Thai version) includes parallel child self-report and parent proxy-report in relation to their children; as directed by the PedsQL™ manual. This instrument comprises an 8-item physical health summary score (physical functioning) and a 15-item psychosocial health summary score (school, social and emotional functioning) that are designed to measure the core dimensions of health with developmentally appropriate forms for ages 2-4, 5-7, 8-12 and 13-18 years. Each item uses 5-point rating scales from 0 to 4, labeled "Never/Almost never/ Sometimes/Often/Almost always". Before analysis, the raw score on each scale was transformed to a 0-100 scale, with higher scores representing better QOL. User agreement was signed with MAPI Research Institute, Lyon, France prior to using the questionnaires. Written informed consent for enrollment in the study was obtained from their parents or legal guardians and oral consent from the children. The study protocol was approved by the Ethics Committee of the Faculty of Medicine, Thammasat University.

### *Statistical analysis*

All analyses were performed using Microsoft Excel 2003 and SPSS for Windows (Statistical Package for the Social Sciences version 17.0, SPSS Inc., Chicago, IL, USA). Data were expressed as mean (SD; standard deviation of mean), median (range) or percentage. Differences in variables between the groups were analyzed by ANOVA, t-test or Mann-Whitney U test for continuous variables and by Chi-square or Fisher's Exact test for categorical variables where appropriate. Internal reliability was assessed using Cronbach's alpha for each of the summary and total scores of the PedsQL™. We used Pearson's or Spearman's rank correlation coefficients as appropriate to examine the strength of the relation between preference values. A multiple linear regression analysis was undertaken, using the forward stepwise technique, to identify independent predictors of HRQOL. Candidate variables were entered into the model with a p-value less than 0.05, while the p-value for backward elimination was set at 0.1. Continuous variables were either included as dichotomous variables or in their original form in the final model depending on the strength of association. The stepwise multiple linear regression analysis was completed for the two outcomes: total summary scores of child self-report and parent proxy-report. All p-values were two-tailed, $p < 0.05$ was considered statistically significant.

## Results

Seventy-five pediatric patients (40 males and 35 females) receiving treatment at Thammasat University Hospital were approached out of ninety-nine on the record. All of them answered and responded to the questionnaires, giving a 100% response rate. Socio-demographic factors and clinical characteristics of the 75 thalassemic children were summarized in Table 1. The mean age at diagnosis and age at the study were 3.6 (0.4) years (range: birth to 14 years) and 7.6 (0.5) years (range:2 to 18 years), respectively. Most patients were studying in secondary school (32%). Regarding

**Table 1.** Patient characteristics

| | Total (n) | n (%)/Mean (SD) |
|---|---|---|
| Socio-economic factors | | |
| Age (years) | 75 | 7.6 (0.5) |
| Gender | 75 | |
| Male | | 40 (53.3%) |
| Female | | 35 (46.7%) |
| Education level | 75 | |
| Not attending school | | 11 (14.7%) |
| Primary school | | 23 (31.7%) |
| Secondary school | | 24 (32.0%) |
| Diploma degree | | 16 (21.3%) |
| Bechelor degree | | 1 (1.3%) |
| Household income (THB per month) | 75 | |
| <10,000 | | 17 (22.7%) |
| 10,000-25,000 | | 37 (49.3%) |
| >25,000-50,000 | | 17 (22.7%) |
| >50,000 | | 4 (5.4%) |
| Type of payment | 75 | |
| Self-payment | | 35 (46.7%) |
| Universal Health Coverage Scheme (UC) | | 22 (29.3%) |
| Civil Servant Medical Benefit Scheme (CSMBS)/ Reimbursement | | 18 (24%) |
| Clinical characteristics | | |
| Type of diagnosis | 75 | |
| Homozygous β-Thalassemia | | 3 (4.0%) |
| β-thalassemia/hemoglobin E | | 28 (37.3%) |
| Hemoglobin H disease (+/Hemoglobin cs) | | 25 (33.3%) |
| AE Bart's disease | | 3 (4.0%) |
| Homozygous Hemoglobin E | | 16 (21.3%) |
| Age at diagnosis (years) | 75 | 3.6 (0.4) |
| Age at first transfusion (years) | 75 | 3.9 (0.5) |
| Baseline hemoglobin (g/dL) | 75 | 9 (0.2) |
| Frequency of blood transfusion | 75 | |
| None | | 24 (32.0%) |
| Occasional (< 8 times/year) | | 25 (33.3%) |
| Regular (> 8 times/year) | | 26 (34.7%) |
| Iron-chelation therapy | 75 | |
| No | | 62 (82.7%) |
| Oral medication* | | 4 (5.3%) |
| Combined subcutaneous and oral medication** | | 9 (12%) |
| Serum ferritin level (during the recent year) | 26 | |
| Mean (ng/mL) | | 790.5 (476.4) |
| <1,000 ng/mL | | 19 (73.1%) |
| ≥1,000 ng/mL | | 7 (26.9%) |
| Complication | 75 | |
| Absent | | 69 (92%) |
| Present | | 6 (8%) |

Values are expressed as mean (standard deviation; SD), frequency (%), *Oral deferiprone tablet, **Combined desferrioxamine infusion and oral deferiprone tablet

the types of payment, approximately 47% of patients were self-payment, while only 30% of them were covered by Universal Health Coverage Scheme (UC). Moreover, about 23% of patients came from families with household income of less than THB 10,000. With respect to clinical features, we found more patients with β-thalassemia/hemoglobin E (37.3%) and hemoglobin H (HbH) disease (33.3%), than β-thalassemia major (4%) and homozygous hemoglobin E (HbE) disease (21.3%). Only 5 patients (0.7%) have undergone splenectomy. One-third of patients had received regular blood transfusion, while 17.3% of them had received iron-chelation therapy. Mean baseline Hb level (SD) was 9 (0.2) g/dL, while mean serum ferritin level (SD) was 790.5 (476.4) ng/mL. Only 8% of the patients reported having complications: gall stones with cholecystitis (2.6%), autoimmune hemolytic anemia (2.6%), chronic active hepatitis C (1.3%) and delayed puberty (1.3%).

The HRQOL scores based on child self-report and parent proxy-report were illustrated in Table 2 which summarized physical health summary (PHS), psychosocial health summary (PCHS) and total summary score (TSS). The reliability of the PedsQL questionnaire in children with thalassemia was well acceptable as evidenced by a Cronbach's alpha greater than 0.7 (0.899 and 0.937 for TSS from child self-report and parent proxy-report, respectively). Mean (SD) of the TSS scores were 78.50 (2.05) for self and 73.41 (2.22) for proxy-report. Overall comparisons, self-report PedsQL™ scores were statistically significantly higher for TSS, PHS and PCHS (all at $p < 0.001$ level; data not shown) than their parents did. However, statistically significant parent-child correlations were found for all of these three summary scores of PedsQL™ ($r = 0.563$-$0.753$; all at $p < 0.001$ level).

The comparison of HRQOL scores (for child self-report and parent proxy-report) across socio-demographic factors and clinical characteristics of the patients were presented in Table 3 and 4, respectively. As shown in Table 3, household income and type of payment were significantly associated with TSS of self-report ($p = 0.010$ and $p = 0.006$, respectively). Children who had lower household income or UC coverage had significant lower scores than those of children who did not. For parents' perspectives, patients who were younger/pre-school age and self-payment had better total HRQOL scores compared to those who were older/school-age or UC coverage ($p = 0.035$, 0.033 and $< 0.001$, respectively). Based on clinical characteristics, disease severity, age at diagnosis, baseline Hb, transfusion therapy and iron-chelation therapy were significantly related with self-reported TSS ($p = 0.014$, 0.010, 0.003, 0.005 and 0.017, respectively) as indicated in Table 4. In addition, disease severity, baseline Hb, transfusion therapy and iron-chelation therapy were also associated with parent-rated TSS ($p = 0.026$, 0.011, $< 0.001$ and 0.008, respectively). This study indicated that patients who were classified as having a severe condition, lower baseline Hb, receiving regular transfusion and combined iron-chelation therapy had significantly low HRQOL scores.

The forward stepwise multiple linear regression analysis was applicable to examine factors affecting the summary HRQOL scores of child self-report and parent proxy-report; as shown in Table 5 and 6, respectively. It indicated that child self-reported HRQOL was negatively predicted by lower household income, early age at diagnosis before 2 years and UC coverage ($p=0.003$, 0.005 and 0.043, respectively). These three variables could help to predict the self-reported HRQOL for 33.2% ($R = 0.639$, $R^2 = 0.408$, $p < 0.001$). The negative predictors of parent proxy-reported HRQOL were regular transfusion therapy, while a positive relationship also found between self-payment and HRQOL ($p = 0.026$ and 0.028, respectively). These two factors could help to predict the proxy-reported HRQOL for 25.8%. ($R = 0.546$, $R^2 = 0.298$, $p < 0.001$).

**Table 2.** PedsQL™ 4.0 quality of life scores and correlation among child self-report and parent proxy-report

| Scale | Child self-report (n = 54) Mean (SD) | Parent proxy-report (n = 75) Mean (SD) | Pearson's correlation coefficient r ($p < 0.001$*) |
|---|---|---|---|
| Total summary score | 78.50 (2.05) | 73.41 (2.22) | 0.741 |
| Physical health summary | 79.63 (2.34) | 72.21 (2.58) | 0.563 |
| Psychosocial health summary | 77.38 (2.28) | 74.61 (2.15) | 0.753 |

Values are expressed as mean (standard deviation; SD) and Pearson's correlation coefficient, r
Statistical method used: Pearson's correlation; *$p < 0.05$ was considered statistically significant

**Table 3.** Quality of life scores of child self-report and parent proxy-report classified by socio-economic factors

| | Child self-report (n = 54) | | | Parent proxy-report (n = 75) | | |
|---|---|---|---|---|---|---|
| | TSS Mean (SD) | PHS Mean (SD) | PCHS Mean (SD) | TSS Mean (SD) | PHS Mean (SD) | PCHS Mean (SD) |
| Socio-econimic factors | | | | | | |
| Age (years) (n = 75) | | | | | | |
| 2-4 (n = 21) | NA | NA | NA | 83.13 (19.33) | 82.89 (22.36) | 83.38 (18.24) |
| 5-7 (n = 21) | 78.40 (17.26) | 78.87 (19.39) | 77.94 (19.79) | 70.71 (17.92) | 67.71 (18.36) | 73.73 (19.72) |
| 8-12 (n = 21) | 78.89 (12.43) | 76.83 (13.57) | 77.38 (2.28) | 66.60 (17.23) | 65.18 (22.67) | 68.02 (16.09) |
| 13-18 (n = 12) | 78.00 (16.46) | 78.65 (18.55) | 77.36 (17.53) | 73.03 (20.02) | 73.79 (23.48) | 72.36 (17.77) |
| p-value | 0.987 | 0.906 | 0.978 | 0.035* | 0.047* | 0.054 |
| Gender (n = 75) | | | | | | |
| Male (n = 40) | 76.12 (13.80) | 76.29 (17.39) | 75.92 (15.04) | 81.28 (16.25) | 83.50 (16.40) | 79.07 (18.75) |
| Female (n = 35) | 73.68 (17.72) | 73.52 (20.87) | 73.85 (18.12) | 73.10 (21.08) | 70.71 (24.10) | 75.49 (19.43) |
| p-value | 0.147 | 0.111 | 0.233 | 0.979 | 0.81 | 0.741 |
| Education level (n = 75) | | | | | | |
| Pre-school (n = 34) | 81.35 (13.15) | 82.45 (14.96) | 80.26 (15.90) | 83.13 (19.33) | 77.48 (21.73) | 81.30 (18.39) |
| Primary school (n = 24) | 78.13 (16.55) | 79.04 (18.92) | 77.22 (18.44) | 70.71 (17.92) | 63.67 (22.15) | 69.17 (17.39) |
| Secondary school and higher (n = 17) | 76.85 (14.81) | 78.31 (16.88) | 75.39 (15.57) | 66.60 (17.23) | 73.71 (21.34) | 68.92 (17.29) |
| p-value | 0.718 | 0.793 | 0.74 | 0.033* | 0.063 | 0.016* |
| Household income (THB per month) (n = 75) | | | | | | |
| < 10,000 (n = 17) | 68.40 (18.02) | 70.63 (17.00) | 66.17 (22.95) | 70.31 (21.30) | 71.32 (23.47) | 69.29 (20.70) |
| 10,000-25,000 (n = 37) | 77.73 (14.46) | 78.68 (18.62) | 76.79 (13.73) | 71.53 (18.53) | 69.85 (22.21) | 73.22 (17.68) |
| > 25,000 (n = 21) | 86.17 (9.96) | 86.91 (11.48) | 85.42 (13.62) | 79.23 (18.33) | 77.08 (21.90) | 81.38 (17.40) |
| p-value | 0.010* | 0.054 | 0.014* | 0.26 | 0.493 | 0.112 |
| Type of payment (n = 75) | | | | | | |
| Self-payment (n = 35) | 82.53 (17.19) | 83.24 (18.61) | 81.82 (19.31) | 82.41 (17.72) | 82.41 (19.25) | 82.40 (18.16) |
| Universal Health | 69.10 (10.39) | 69.67 (15.62 | 68.53 (10.73) | 60.99 (16.13) | 58.95 (19.82) | 63.03 (14.57) |
| Coverage Scheme (UC) (n = 22) | | | | | | |
| Civil Servant Medical Benefit Scheme | 83.26 (11.66) | 85.63 (11.74) | 80.89 (15.33) | 71.41 (16.97) | 68.58 (22.08) | 73.62 (17.02) |
| (CSMBS)/Reimbursement (n = 18) | | | | | | |
| p-value | 0.006* | 0.011* | 0.028* | < 0.001* | < 0.001* | < 0.001* |

Values are expressed as mean (standard deviation; SD), Statistical method used: One-way ANOVA; *p < 0.05 was considered statistically significant, NA, not applicable

**Table 4.** Quality of life scores of child self-report and parent proxy-report classified by clinical characteristics

| | Child self-report (n = 54) | | | Parent proxy-report (n = 75) | | |
|---|---|---|---|---|---|---|
| | TSS Mean (SD) | PHS Mean (SD) | PCHS Mean (SD) | TSS Mean (SD) | PHS Mean (SD) | PCHS Mean (SD) |
| Clinical characteristics | | | | | | |
| Type of diagnosis (n = 75) | | | | | | |
| Severe (n = 31) | 72.23 (12.16) | 71.20 (18.17) | 73.26 (11.05) | 66.34 (19.12) | 64.52 (23.23) | 68.16 (17.09) |
| Moderate (n = 28) | 81.25 (15.94) | 83.95 (14.18) | 78.56 (20.59) | 78.32 (17.95) | 78.68 (19.13) | 77.96 (19.37) |
| Mild/asymptomatic (n = 16) | 87.81 (15.11) | 90.63 (11.16) | 85.00 (17.22) | 78.52 (18.36) | 75.78 (22.52) | 81.25 (17.30) |
| p-value | | | | | | |
| Age at diagnosis (years) (n = 75) | | | | | | |
| < 2 (n = 24) | 69.33 (11.97) | 70.09 (17.37) | 68.57 (10.42) | 71.99 (20.53) | 73.33 (22.59) | 70.65 (20.45) |
| 2-5 (n = 25) | 78.88 (15.64) | 80.11 (16.69) | 77.65 (18.80) | 73.04 (18.79) | 68.75 (22.14) | 77.34 (17.53) |
| > 5 (n = 26) | 85.17 (13.90) | 86.46 (14.81) | 83.89 (15.77) | 76.22 (18.61) | 76.04 (22.66) | 76.39 (17.29) |
| p-value | 0.010* | 0.024* | 0.034* | 0.766 | 0.529 | 0.363 |
| Baseline hemoglobin (g/dL) (n = 75) | | | | | | |
| < 7 (n = 8) | 70.10 (15.00) | 68.30 (19.55) | 71.90 (15.41) | 68.27 (18.39) | 67.97 (23.55) | 68.57 (14.86) |
| 7-9 (n = 27) | 72.03 (13.97) | 74.50 (15.21) | 69.56 (15.63) | 65.86 (18.17) | 65.05 (21.02) | 66.67 (17.30) |
| > 9 (n = 40) | 84.99 (13.20) | 85.94 (15.69) | 84.05 (15.48) | 79.54 (18.36) | 77.89 (21.90) | 81.18 (18.00) |
| p-value | 0.003* | 0.011* | 0.007* | 0.011* | 0.057 | 0.004* |
| Frequency of blood transfusion (n = 75) | | | | | | |
| None (n = 24) | 85.93 (11.50) | 86.13 (17.60) | 85.73 (12.32) | 79.26 (18.24) | 77.47 (23.20) | 81.04 (17.70) |
| Occasional (< 8 times/year) (n = 25) | 80.89 (17.00) | 84.55 (14.04) | 77.22 (20.91) | 80.63 (16.90) | 80.88 (16.98) | 80.39 (17.88) |
| Regular (> 8 times/year) (n = 26) | 70.42 (12.24) | 70.00 (15.65) | 70.83 (13.03) | 61.07 (16.45) | 59.01 (20.51) | 63.13 (14.91) |
| p-value | 0.005* | 0.005* | 0.027* | < 0.001* | < 0.001* | < 0.001* |
| Iron-chelation therapy (n = 75) | | | | | | |
| No (n = 62) | 81.47 (14.91) | 83.91 (15.66) | 79.02 (17.91) | 76.33 (18.88) | 75.30 (22.05) | 77.35 (18.34) |
| Oral medication** (n = 4) | 76.15 (17.86) | 78.13 (17.68) | 74.17 (18.38) | 68.02 (19.79) | 65.63 (22.82) | 70.42 (18.38) |
| Combined subcutaneous and oral medications*** (n = 9) | 66.03 (7.04) | 60.76 (10.61) | 71.30 (8.53) | 55.71 (11.03) | 53.82 (15.21) | 57.59 (11.31) |
| p-value | 0.017* | 0.001* | 0.430 | 0.008* | 0.020* | 0.009* |

Values are expressed as mean (standard deviation; SD), Statistical method used: One-way ANOVA; *p < 0.05 was considered statistically significantType of diagnosis: 1) *Severe*, Homozygous β-Thalassemia, β-thalassemia/hemoglobin E; 2) *Moderate*, Hemoglobin H disease (+/Hemoglobin cs), AE Bart's disease; 3) *Mild/asymptomatic*, Homozygous hemoglobin E**Oral deferiprone tablet; ***Combined desferrioxamine infusion and oral deferiprone tablet

**Table 5.** Stepwise multiple linear regressions predicting quality of life scores on the subscales of PedsQL™ 4.0 of child self-report

| | Total summary scores (TSS) | | | | Physical health summary (PHS) | | | | Psychosocial health summary (PCHS) | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | β | SE (β) | t | p-value | β | SE (β) | t | p-value | β | SE (β) | t | p-value |
| Child self-report | | | | | | | | | | | | |
| Household income <10,000 THB per month | -15.832 | 5.056 | -3.131 | 0.003 | - | - | - | - | - | - | - | - |
| Age at diagnosis < 2 years | -13.393 | 4.554 | -2.941 | 0.005 | -12.67 | 5.291 | -2.394 | 0.021 | | | | |
| Covered by Universal Health Coverage Scheme | -9.412 | 4.525 | -2.08 | 0.043 | - | - | - | - | -12.359 | 5.647 | -2.189 | 0.033 |
| Combined iron-chelation therapy | - | - | - | - | -20.76 | 5.475 | -3.793 | < 0.001 | - | - | - | - |

Values are expressed as unstandardized coefficient; β and standard error of β; SE (β), Statistical method used: Stepwise multiple regression analysis, TSS model: R = 0.639, $R^2$ = 0.408, p-value < 0.001, PHS model: R = 0.576, $R^2$ = 0.332, p-value < 0.001, PCHS model: R = 0.362, $R^2$ = 0.131, p-value <0.028

**Table 6.** Stepwise multiple linear regressions predicting quality of life scores on the subscales of PedsQL™ 4.0 of parent proxy-report

| | Total summary scores (TSS) | | | | Physical health summary (PHS) | | | | Psychosocial health summary (PCHS) | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | β | SE (β) | t | p-value | β | SE (β) | t | p-value | β | SE (β) | t | p-value |
| Parent proxy-report | | | | | | | | | | | | |
| Self-payment | 10.999 | 4.989 | 2.245 | 0.028 | - | - | - | - | -16.597 | 4.563 | -3.637 | 0.001 |
| Regular transfusion (> 8 times/year) | -13.478 | 5.905 | -2.282 | 0.026 | -18.46 | 5.76 | -3.205 | 0.002 | - | - | - | - |
| Pre-school level | - | - | - | - | - | - | - | - | 10.974 | 4.794 | 2.289 | 0.025 |

Values are expressed as unstandardized coefficient; β and standard error of β; SE (β), Statistical method used: Stepwise multiple regression analysis, TSS model: R = 0.546, $R^2$ = 0.298, p-value < 0.001, PHS model: R = 0.438, $R^2$ = 0.192, p-value < 0.001, PCHS model: R = 0.549, $R^2$ = 0.301, p-value < 0.001

**Discussion**

In this cross-sectional single-institution study of HRQOL in Thai children with thalassemia, we selected the PedsQL™ 4.0 as HRQOL instruments to measure the unique perspectives of children and their parents; since these perspectives may be independently related to various physical and psychosocial variables. The study demonstrated that information provided by proxy-respondents is not equivalent to which reported by the patients, as it is well documented in literatures[13,14]. However, there was concordance between parents and children, in terms of rating scale in our study. Also, it was slightly higher internal consistency reliability on parent proxy-report, as compared to child-report (0.937 vs. 0.899). While child self-report should be considered for measuring HRQOL, our findings emphasized the fundamental and reliable roles for parent proxy-report in pediatric clinical trials and QOL studies; especially in circumstances when children are too young, too cognitively impaired or too ill to complete a HRQOL instrument.

The HRQOL self-assessment in this study showed that psychosocial health had a lower score than physical health, the same pattern as the previous study[7,10]. In addition, as the previous studies[15-17], parent-rated HRQOL scores were significantly lower than those of their child-rated. It is possible that frequent school missing and suffering from chronically disability condition had a negative impact on children's perspective. Moreover, parents were concerned about their children's illness and future health, including the health care cost. Comparison to recent report on HRQOL of healthy Thai adolescents[18], mean PedsQL™ scores (SD) was found to be comparable to the total scores (TSS) obtained from this study [78.50 (2.05) vs. 77.20 (10.50)]. However, our scores were slightly lower in physical health [79.63 (2.34) vs. 81.59 (12.53)], while there was higher in psychosocial health [77.38 (2.28) vs. 74.87 (14.39)]. However, it might be limitation of comparison due to different age group; that contributed to different health perceptions and needs. Direct comparison to previous study on HRQOL of Thai thalassemic children and adolescents[10], the HRQOL scores were not much different. Nevertheless, the scores were found to be significant difference, compared to Malaysian children with thalassemia[7]. Thai children with thalassemia from the present and previous studies[10] had much higher HRQOL scores than Malaysian children with thalassemia. It could be explained by the difference in disease severity and treatment of patient. More than 50% of patients in the Malaysian study were diagnosed with homozygous β-thalassemia, and about 80% were transfusion-dependent. While only 4% of patients were diagnosed with homozygous β-thalassemia, and 35% were transfusion-dependent in the present study. Furthermore, possible reasons were revealed that there were differences in cultures, experiences and perspectives between Thai and Malaysian.

To analyze the predictors of HRQOL using multiple regression, the study outlined the basic sharing between perspectives of children and their parents. Severe conditions (in terms of early onset of disease presentation and transfusion dependence), low household income and UC coverage were negatively predicted child HRQOL from both of child-reported and parent-reported HRQOL summary scores. For the psychosocial health predictors, our finding underscored that younger age was related to better PCHS of parent-reported HRQOL. While, other child-reported HRQOL studies revealed that older age was positively predicted HRQOL[7,10]. One explanation is that parents express a high degree of concern and frustration regarding their pre-teen and teen's well-being. Parents usually take an important role in decision-making of what they believe to be the best for their child; however teenage needs more independent lifestyle. These points lead to be misunderstanding and confliction between their views and interpretations on QOL. For physical health predictors, it was similar to the previous studies[6,8,10,19], PHS of child-rated HRQOL was negatively predicted by combined oral and subcutaneous iron-chelation therapy, due to the burden of nightly subcutaneous injections of desferrioxamine plus daily oral deferiprone tablet. It could be the fact that severe cases (patients with transfusion dependence and iron overload) probably need combined iron-chelation therapy to achieve serum ferritin levels below 1,000-1,500 ng/mL[20-22], a threshold that is known to be the most accessible tool and associated with a reduced risk of iron overload-related complications (*e.g.* heart failure) in patients with thalassemia. However, there were no significant correlations between serum ferritin level and each domain on the PedsQL™ in the present study and previous study[10]. The reason might be too small sample size and proportion of transfusion-dependent patients in this study.

Since the disease severity and treatment were not always associated with reductions in the HRQOL, as the previous literature; this study is the first report showing a significant relationship between the HRQOL

and family financial impact in children with thalassemia. Unexpectedly, type of payment had an impact on both children and parents' perspectives. We can only attempt to explain for our subjects. Self-payment could be implied to be higher household income and affordable medical expense; which assisted to predict the better parent-rated HRQOL. Whereas, patients who were under UC program might be underprivileged subgroups and affecting the patient's overall well-being.

Certain limitations of this study should be noted. First, because this study was a cross-sectional design, we cannot refer to inferring causal paths or evaluating any interventions. Second, because of the absence of HRQOL scores of healthy children in Thailand with matching on age and sex for comparison; therefore, the true impact of thalassemia syndrome on HRQOL was hardly estimated. Third, we did not collect data about the family caregivers' characteristics and their affecting QOL. Because scanty research has been directed at evaluating strategies for preserving caregivers' well-being, it is very worthwhile to identify predictors of caregiver QOL. Forth, in this single-institution study, sample size may be inadequate and potential limitation of the study.

Despite limitations, the study contributes to the existing literature on a biopsychosocial predictor that is prevalent in children with thalassemia and that may contribute to disparities in child QOL. In addition, data provide further evidence of the need to 1) routinely assess their HRQOL for both of transfusion-dependent and non-transfused thalassemia patients; 2) facilitate the school-age patient by offering the weekend clinic/ treatment to prevent from frequent missing from school; 3) promote the optimal treatment for severe cases, in order to receive regular transfusion and adequate iron chelation; 4) consider to manage thalassemia disease in Thailand under the disease management program for development of efficient treatment and patient care regimens. Further extended longitudinal research and larger sample size are required to gain better understanding of the HRQOL status and predictors for the long-term outcomes. In addition, matched control analysis and QOL assessment of their family caregivers are emphasized to identify the special needs as well as health care services to promote the best possible QOL and well-being of thalassemia patients.

## Conclusion

Although improving a patient's prognosis may be the main goal of pediatricians, improving the QOL is also important for pediatric patients. We determined physical health, psychosocial health and total summary HRQOL scores, as well as various biopsychosocial predictors of these three summary PedsQL™ scores. Severe conditions, low household income and UC coverage were negatively predicted child HRQOL; with in concordance between child-report and parent-report. Modification of thalassemia management program to be more comprehensive and patient-oriented could be beneficial for the patients and their family.

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## Conflict of interest

The authors indicated no potential conflicts of interest.

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## ปัจจัยทางกายภาพ จิตใจ และสังคมที่มีผลต่อคุณภาพชีวิตของผู้ป่วยเด็กโรคธาลัสซีเมียในโรงพยาบาลธรรมศาสตร์เฉลิมพระเกียรติ

**พชรพรรณ สุรพลชัย, วัลลี สัตยาศัย, ผกาทิพย์ ศิลปะมงคลกุล, อุมาพร อุดมทรัพยากุล**

***วัตถุประสงค์***: *ศึกษาคุณภาพชีวิตที่เกี่ยวข้องกับสุขภาพ และปัจจัยที่สัมพันธ์กับคุณภาพชีวิตของผู้ป่วยเด็กโรคธาลัสซีเมีย ที่มารับการรักษาที่โรงพยาบาลธรรมศาสตร์เฉลิมพระเกียรติ*

***วัสดุและวิธีการ***: *ทำการศึกษาในผู้ป่วยเด็กโรคธาลัสซีเมีย อายุ 2-18 ปีที่มารับการรักษาที่โรงพยาบาล ธรรมศาสตร์เฉลิมพระเกียรติ โดยใช้แบบบันทึกข้อมูลทางคลินิก และแบบสอบถามคุณภาพชีวิตสำหรับผู้ป่วยเด็ก (PedsQL™) ฉบับภาษาไทย เพื่อประเมินในมุมมองของทั้งผู้ป่วยเด็กและผู้ปกครอง*

***ผลการศึกษา***: *ค่าเฉลี่ย (ค่าเบี่ยงเบนมาตรฐาน) ของคะแนนคุณภาพชีวิตโดยรวมทั้งจากการประเมินของผู้ป่วยเด็กและผู้ปกครอง ได้แก่ 78.50 (2.05) และ 73.41 (2.22) ตามลำดับ ซึ่งมีคะแนนอยู่ในระดับสูงใกล้เคียงกับประชากรเด็กทั่วไป ปัจจัยที่มีผลทำนายคุณภาพชีวิต ได้แก่ การมีรายได้ของครอบครัวน้อยกว่า 10,000 บาทต่อเดือน การที่ได้รับการวินิจฉัยตั้งแต่อายุน้อยกว่า 2 ปี และการใช้สิทธิบัตรประกันสุขภาพถ้วนหน้า เป็นปัจจัยที่ร่วมกันทำนายผลในทางลบต่อคุณภาพชีวิตโดยรวมจากการประเมินของผู้ป่วยเด็ก ส่วนปัจจัยที่มีผลร่วมกันในการทำนายคุณภาพชีวิตโดยรวมจากการประเมินของผู้ปกครอง ได้แก่ การที่ต้องมารับเลือดเป็นประจำทุก 1-2 เดือน และการจ่ายค่ารักษาพยาบาลเอง โดยการมารับเลือดประจำมีผลในทางลบ ตรงกันข้ามกับการจ่ายค่ารักษาเองที่มีผลในทางบวกต่อคุณภาพชีวิต*

***สรุป***: *มีหลากหลายปัจจัยที่มีผลทำนายคุณภาพชีวิตของผู้ป่วยเด็กโรคธาลัสซีเมียทั้งในด้านความรุนแรงของโรค แนวทางการรักษา ..และเศรษฐานะของครอบครัว ซึ่งปัจจัยเหล่านี้มีผลต่อการวางแผนการดูแลในระยะยาวต่อไปในอนาคต*