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Original Article

Quality of life assessment of children with thalassemia

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Abstract

Background Thalassemia is a chronic disease that is becoming a major health problem in the world, including the Mediterranean, as well as Malaysia, Thailand and Indonesia. This condition clearly affects the patient's quality of life, because of the condition itself and the effects of treatment. Assessment is needed to determine actions to be taken to improve the quality of life in thalassemic children.

Objective To assess the differences in quality of life of thalassemic children compared to their normal siblings.

Methods We performed a cross-sectional study from May 2010 until June 2010 in H. Adam Malik Hospital, Medan and the home of a member of the North Sumatra Chapter of the Association of Parents of Thalassemia Sufferers (Perhimpunan Orangtua Penderita Talasemia Indonesia, POPTI). Thalassemic children aged 5 - 18 years and their age and gender-adjusted siblings were divided into two groups: case group and control group. Parents and children were asked to fill the PedsQL (Pediatric Quality of Life Inventory) version 4.0 questionnaire to assess their quality of life.

Results There were 59 children in each group. The assessments of four quality of life domains in the thalassemic group vs the control group showed the following: physical function 53.1 vs 71.5 (95% CI -21.41 to -15.26, P=0.0001), emotional function 50.9 vs 62.9 (95% CI -16.82 to -7.41, P=0.0001), social function 62.5 vs 72.8 (95% CI-13.50 to -7.01, P=0.0001) and school function 36.2 vs 56.0 (95% CI -22.95 to -16.71, P=0.0001). Total scores were 50.9 vs 66.1 (95% CI -18.20 to -13.12, P=0.0001). School function was the most affected parameter studied, with thalassemic children scoring lower than the control group.

Conclusion There were significant decreases in the quality of life parameters in the thalassemic group compared to the control group. Thalassemic children have poorer quality of life compared to their normal siblings, with school function being the most affected domain. **[Paediatr Indones. 2011;51:163-9]**.

Keywords: *thalassemia, normal siblings, quality of life, PedsQL*

Thalassemia is an inherited hemoglobin disorder that is becoming a major health problem in the world, especially in Mediterranean region, the Middle East, the Indian subcontinent, Southeast Asia, Malaysia, Thailand and Indonesia.[1-3] It has been estimated that approximately 7% of the world population are carriers of such disorders and that 300,000 – 400,000 babies with severe forms of these diseases are born each year (WHO, 2001).[4] In North Sumatra, the carrier population reached 7.69%, consisting of 3.35% alpha thalassemia and 4.07% beta thalassemia.[5] Children with thalassemia appear healthy at birth, but develop anemia that becomes progressively worse due to the partial or total absence of hemoglobin.[2] Because of this condition, they need regular blood transfusions for the rest of their lives to manage chronic anemia and hemoglobin levels.[1,5,6] Regular blood transfusions lead to iron accumulation in organs and may disrupt organ function and/or damage organs.[1,2,7,8] Iron overload causes most of the mortality and morbidity associated with thalassemia.[8] Long term transfusions should be accompanied by therapy with iron chelating agents.[9]

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Thalassemia has a negative impact on quality of life due to the effects of the disease and its treatment, not only affecting childrens' physical function, but also their social, emotional, and school function, leading to an impaired quality of life.[2,10] The most commonly affected domains previously reported were feelings of depression, anxiety, psychological problems, emotional burden, hopelessness, difficulty with social integration, and school problems.[2,11,12] Similar conditions also affected their family members, such as sadness, disappointment, hopelessness, stress, depression, and anxiety about their children's lives.[13] The assessment of quality of life in thalassemic children and their family members is important in order to determine actions to be taken to improve quality of life. The aim of this study was to assess differences in quality of life of thalassemic children compared to their normal siblings.

Methods

We conducted a cross-sectional study from May - June 2010 in Adam Malik Hospital, Medan and the home of one of North Sumatra's POPTI members. We included children aged 5 - 18 years of all thalassemia classifications and their normal siblings, with age at onset of anemia < 2 years, and age at first transfusion < 4 years, as well as pre-transfusion hemoglobin level < 7 g/dL. Parents and children gave informed, written consent, and filled questionnaires completely. We excluded children with cognitive function problems, psychotic problems and cancer.

Subjects were divided into two groups: the thalassemic group and their normal siblings group. We measured anthropometric values of each child before the study began. Weight was measured with Camry® scales and height was measured with a Microtoise 2M stature meter.

Parents and children were asked to fill the PedsQL version 4.0 questionnaires after receiving directions and explanations on the meaning of each question. We collected and reviewed questionnaire sheets after they were completely filled. The completed questionnaires were adjusted for age and gender. Data for each domain (physical, emotional, social, and school functions) were tabulated. Children with significantly poor quality of life were referred to a child psychologist.

In this study, quality of life assessment was performed using the Pediatric Quality of Life Inventory (PedsQL) 4.0 Generic Core Scale. This questionnaire includes parallel child self-reports (age ranges 2-4, 5-7, 8-12, and 13-18 years). PedsQL items ask how much of a problem a particular issue has been for patients during a certain period. Item responses are measured on a five-point rating scale, ranging from 0 (never a problem) to 4 (almost always a problem). The 23 items consist of 8 items on physical function, 5 items on emotional function, 5 items on social function, and 5 items on school function, yielding a total score. Each scale has a score ranging from 0-100, with higher scores indicating higher quality of life.

This study was approved by the Medical Ethics Committee of the University of Sumatra Utara Medical School.

We used SPSS version 14.0 and Microsoft Excel 2007 for data processing. Independent t test was used to compare differences in quality of life between the two groups. Differences were considered significant at $P < 0.05$, and a 95% CI.

Results

Thalassemic children and their normal siblings were recruited to this study. There were 136 children, 68 with thalassemia and 68 normal siblings. Out of 136 children, 18 children were excluded from this study because 4 children were below 5 years of age, 5 children were more than 18 years of age, 2 children had mental retardation, and 7 children had no siblings. The 118 children who fulfilled the inclusion criteria were devided into two groups: 59 thalassemic children or case group, and 59 normal siblings or control group.

The average age in both groups was 10.5 years, most commonly boys (67.8%). The nutrition status of both groups was normal and the most common level of education was primary school. Most common parents' education level was high school with self-owned business as their main profession. (**Table 1**)

Table 2 shows the hematologic profile of the thalassemic children. This profile was consistent with the thalassemia condition. We found the most common age at onset of anemia was ≤ 2 years

(96.6%). The most common age at first diagnosis of thalassemia was > 2 years (52.5%), with most having beta thalassemia major (96.6%). The most common age at first transfusion was < 4 years (96.6%), with a pre-transfusion hemoglobin level of < 7 g/dL (96.6%).

Our data also showed that 30.5% of thalassemic subjects had parents who were both carriers. In 10.2% of subjects only one parent was a carrier and in 59.3% of subjects it was unknown which parents were carriers. Routine transfusions were given to 91.5% of subjects every month, most commonly with 3 bags (49.2%). Routine iron chelating therapy was given to 78% of the thalassemic children.

Table 1. Baseline characteristics of subjects

Characteristic	Thalassemia patients (n=59)	Normal siblings (n=59)
Mean age, years (SD)	10.56 (3.14)	10.56 (3.14)
Sex, n (%)		
Boy	40 (67.8)	40 (67.8)
Girl	19 (32.2)	19 (32.2)
Mean weight, kg (SD)	27.88 (9.10)	29.32 (9.96)
Mean height, cm (SD)	131.37 (15.36)	133.75 (16.32)
Nutritional status, n (%)		
Moderate malnutrition	1 (1.7)	0
Mild malnutrition	8 (13.6)	9 (15.3)
Normal	50 (84.7)	49 (83.0)
Overweight	0	1 (1.7)
Child's level of education, n (%)		
Did not attend school	6 (10.2)	0
Kindergarten	11 (18.6)	11 (18.6)
Primary school	29 (49.2)	32 (54.2)
Elementary school	8 (13.6)	11 (18.6)
High school	5 (8.5)	5 (8.5)
Parents' level of education, n (%)		
Primary school	12 (20.3)	16 (27.1)
Elementary school	4 (6.8)	6 (10.2)
High school	35 (59.3)	30 (50.8)
Diploma	2 (3.4)	2 (3.4)
Bachelor's degree	6 (10.2)	5 (8.5)
Parents occupation, n (%)		
Employees	12 (20.3)	12 (20.3)
Own business	47 (79.7)	47 (79.7)

Table 3 shows there were significant differences of quality of life between thalassemic children and their normal siblings. Assessments of the four quality of life domains in the thalassemic vs control groups showed the following: physical function 53.1 vs 71.5

Table 2. Hematologic profile of thalassemic children

Characteristic	n (%)
Age at onset of anemia	
0	2 (3.4)
≤ 2 years	57 (96.6)
Age at first diagnosis of thalassemia	
≤ 2 years	28 (47.5)
> 2 years	31 (52.5)
Parents as carrier	
Unknown	35 (59.3)
1 carrier	6 (10.2)
2 carriers	18 (30.5)
Type of thalassemia	
Beta major	57 (96.6)
Beta minor	2 (3.4)
Age at first transfusion	
Never transfused	2 (3.4)
≤ 2 years	24 (40.7)
3 years	33 (55.9)
Number of transfusions per month	
0	2 (3.4)
≤ 2 bags*	21 (35.6)
3 bags*	29 (49.2)
4 bags*	5 (8.5)
≥ 5 bags*	2 (3.4)
Routine transfusion	
No	5 (8.5)
Yes	54 (91.5)
Mean pre-transfusion hemoglobin level	
Not examined	2 (3.4)
≤ 4 g/dL	5 (8.5)
5 g/dL	10 (16.9)
6 g/dL	42 (71.2)
Ferritin serum level	
Not examined	2 (3.4)
< 1000 µg/L	11 (18.6)
> 1000 µg/L	6 (10.2)
> 2000 µg/L	40 (67.8)
Iron chelation therapy	
No	13 (22)
Yes	(78)

* Each bag contains 175 mL packed red blood cells

Table 3. Differences in quality of life between thalassemic children and their normal siblings

Quality of life	Case group (n=59) mean (SD)	Control group (n=59) mean (SD)	95% CI	P
Physical function	53.1 (9.49)	71.5 (7.23)	-21.41 to -15.26	0.0001
Emotional function	50.9 (13.96)	62.9 (11.75)	-16.82 to -7.41	0.0001
Social function	62.5 (10.92)	72.8 (6.25)	-13.50 to -7.01	0.0001
School function	36.2 (10.06)	56.0 (6.75)	-22.95 to -16.71	0.0001
Total score	50.9 (7.55)	66.1 (4.35)	-18.20 to -13.12	0.0001

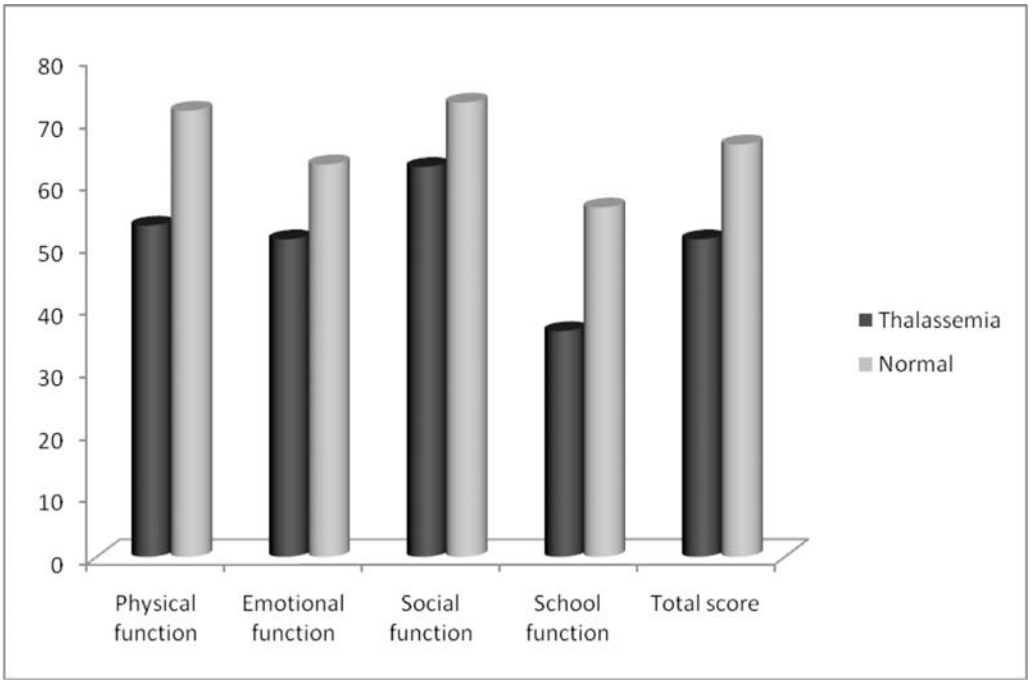

Figure 1. Differences in quality of life between thalassemic children and their normal siblings

(95% CI -21.41 to -15.26, P=0.0001), emotional function 50.9 vs 62.9 (95% CI -16.82 to -7.41, P=0.0001), social function 62.5 vs 72.8 (95% CI -13.50 to -7.01, P=0.0001) and school function 36.2 vs 56.0 (95% CI -22.95 to -16.71, P=0.0001). The total scores were 50.9 vs 66.1 (95% CI -22.95 to -16.71, P=0.0001). School function was most affected parameter (**Figure 1**).

Discussion

We compared the quality of life of thalassemic children to their normal siblings, as representative family members to assess the effects of the disease and its treatment. The assessment of quality of life in children, especially in those with chronic diseases such as thalassemia is important.[2] The negative impact of the disease and its treatment can affect the quality of life of patients and their family members, hence the need to assess both groups.[2,13] The WHO defines quality of life as an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns.[10] It is a broad-ranging concept, affected in a complex way by the person's health, psychological state, personal beliefs, social relationships and their relationship to salient features of their environment.[10,14]

The hematology profile showed 57 (96.6%) of thalassemic patients to have beta thalassemia major with mean age at onset of anemia < 2 years old, pre-transfusion hemoglobin level < 7 g/dL, and age at first transfusion < 4 years old. More than half (52.5%) of the subjects were diagnosed with thalassemia at the age of > 2 years, although they had been anemic before the age of 2 years.

Thalassemia is a chronic disease with serious clinical symptoms. A study in Thailand found several conditions that correlate to the severity of disease in thalassemia patients: age at onset of anemia < 2 years old, age at first transfusion < 4 years old, pre-transfusion hemoglobin level < 7 g/dL, and beta thalassemia major.[6]

We found that of all thalassemic children's parents, 30.5% had both parents as carriers, 10.2% had one parent as a carrier, and 59.3% had unknown parental status. The above results are consistent with thalassemic offspring often having carrier parents. We found 96.6% of the thalassemic children to be

thalassemia major, a condition typically inherited from two carrier parents. There was also a small number of other thalassemic children.

Thalassemia major can often be prevented by avoiding marriage of two carrier parents or by performing prenatal diagnoses in high risk mothers.[5,15] Marriage of two carrier parents results in a 25% chance of producing thalassemic offspring, 50% chance of producing a carrier who can pass on the disease if he/she marries another carrier, and a 25% chance of normal offspring (not thalassemic or carrier).[5,16]

Almost all of the thalassemic subjects (91.5%) received monthly transfusions, with various blood volumes transfused depending on hemoglobin level upon visiting the hospital. The most common amount of blood transfused was 3 bags (49.2% of subjects) and the most common hemoglobin level upon hospital visit was 6 g/dL (71.2%).

In the management of thalassemia, regular red blood cell transfusions can reduce the complications of anemia and ineffective erythropoiesis, permit normal growth and development throughout childhood, and extend survival in thalassemic children.[1,15,17] The decision to initiate regular transfusions is generally based on the observation of a hemoglobin concentration less than 6 g/dL.[1,15]

We found most subjects (84.7%) had a normal nutritional status, which is not in keeping with the theory that children with thalassemia have growth problem. This was caused by the anthropometry data showed abnormal condition (short stature) which in turn resulting in normal nutritional status.

Children with thalassemia are known to have abnormal growth. The etiology of these co-morbidities is typically ascribed to the toxic effect of regular blood transfusions related to iron overload.[3,7,18] Malnutrition is primarily caused by inadequate nutrient intake, as indicated by the capacity to gain weight appropriately when provided with nutritional support in the absence of intestinal malabsorption.[19]

Most subjects in our study (78%) had received iron chelating therapy regularly after blood transfusions, with serum ferritin examinations every 3 months. We found that 10.2% of subjects had serum ferritin > 1000 μg/L and 67.8% had serum ferritin > 2000 μg/L. A few subjects had not received chelating therapy because their serum ferritin was less than 1000 μg/L or they had not been checked yet.

Progressive iron overload is a consequence of ineffective erythropoiesis, increased gastrointestinal absorption of iron and above all, multiple blood transfusions.[20] Every 500 ml of red blood cells transfused contains approximately 250 mg of iron that will circulate in the body, but the body cannot excrete more than 1 mg of iron per day.[20,21] The accumulation of iron results in progressive dysfunction of the heart, liver and endocrine glands.[20,22,23]

Iron chelating agents are needed to control iron levels in patients who receive regular blood transfusions.[1,2,6] Deferoxamine has until now been considered the treatment of choice for patients with chronic iron overload due to blood transfusion.[1,8,24] The time to start the iron chelating agents is determined by the patient's serum ferritin and iron levels, as well as the total iron binding capacity after regular transfusions.[8,20] Chelating therapy is typically started if the serum ferritin level exceeds 1000 μg/L or after receiving 10 - 12 transfusions.[20]

We assessed the quality of life of thalassemic children and their normal siblings with the PedsQL version 4.0 questionaire. In this study, we used the English-Indonesian version of PedsQL 4.0 generic core module in a sample of healthy children and children with thalassemia.

In studies of children's quality of life, there are generally two types of tools that can be used,[25] generic measures and disease-specific measures. Each has its own advantages and disadvantages. Generic measure tools can be used in healthy or sick children with various diseases. Hence, they can be used to compare the quality of life of children with chronic illness to healthy children or children with other types of diseases. The disadvantage of these tools is that they cannot be used to assess specific symptoms of certain illnesses or possible side effects. On the other hand, specific measure tools cannot be used to compare sick children to healthy ones, but they are more sensitive and specific for certain symptoms or side effects of the disease.[14,26]

The choice of the tools depends on the subjects, specific conditions or the illness.[14] The reliability and validity of the tool also determines the validity of the assessment. For practical purposes, the ideal tool must be brief, but retain good reliability and validity, provide useful information, able to be filled by children of various ages and their parents, and be available both in generic and specific measures.[14,26]

PedsQL is a tool recommended for quality of life assessment because it fulfills several criteria for such a valid tool. It has high validity and reliability (has been proven in several studies in children with malignancies, diabetes and heart disease), is available in generic and specific forms for certain diseases (e.g., PedsQL module for cancer, asthma, diabetes, rheumatic heart disease, cerebral palsy, epilepsy and thalassemia), can be filled by children (self-report) or parents/guardians (proxy report), has been translated to several languages to facilitate usage, and is available for various age groups: 2-4 years (proxy report), 5-7 years (self and proxy report), 8-12 years (self and proxy report), as well as 13-18 years (self and proxy report).[27-31]

The original author of PedsQL is Dr. James W. Varni. He has developed and made several modifications since 2001. This tool consists of several versions (version 1.0 until 4.0) with 23 questions in 4 domains of assessment: physical, emotional, social and school domains. The 4.0 version is a generic measures tool. In PedsQL, the quality of life of children with chronic illness may be compared to healthy/normal children as a control.[2,32]

The results of our study are comparable to a previous study where the quality of life of thalassemic children was significantly lower than the control group.[2] Our study also showed the results of each domain in the quality of life assessment: physical, social, emotional and school domain. Similar to the previous study, school domain had the lowest mean score 36.2 (SD 10.06) in the case group.

Studies on quality of life of thalassemic children have been limited, but needed.[2] A study in Malaysia in 2005 and then another in Thailand in 2010 used the PedsQL version 4.0 questionnaire to assess the quality of life of thalassemic children compared to normal children as a control.[2,6] These study reported that the quality of life of thalassemic children was significantly lower comparared to control group.[2,6] Effects of thalassemia on quality of life included physical, social, emotional and school issues. A study in Malaysia reported that school function was the parameter most affected. Thalassemic children are frequently absent from school, since they routinely go to the hospital for blood transfusions and iron chelating therapy.[2]

This is the first study from North Sumatra, Indonesia used to assess quality of life in children with chronic illness, in particular, thalassemia. Our findings supported other studies in Malaysia and Thailand in that it also showed that children with thalassemia have a poorer quality of life. However, we were unable to evaluate if there was any improvement to quality of life after intervention, such as education for parents and consultations with child psychologists. Further study is needed in this area.

In conclusion, we found that thalassemic children had a lower quality of life compared to their clinically normal siblings, with school function the most negatively affected.

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