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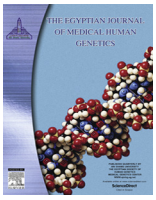

Original article

Evaluation of health-related quality of life and muscular strength in children with beta thalassemia major

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ABSTRACT

Background: Thalassemia is an inherited blood disorder that requires repeated blood transfusions and chelation regimes. This may lead to restrictions in physical activities, social participation as well as decreased muscle strength.
Aim: The aim of this study was to evaluate the health-related quality of life (HRQoL), muscular strength and pain in children with β-thalassemia major.
Patients and method: One hundred and twenty children (60 with β-thalassemia major and 60 age-matched healthy) were participated in a cross-sectional study from both sexes (57 girls and 63 boys) with ages ranging from two to twelve years. HRQoL (physical, emotional, social and school functioning), muscular strength and pain were evaluated for all children by using the pediatric quality of life inventory™ (PedsQL™) 4.0 generic core scale, hand-held dynamometer and visual analogue scale (VAS) respectively.
Results: Children with β-thalassemia major showed a significant decrease in all domains of health-related quality of life and handgrip strength with a significant increase in VAS score ($p \leq 0.0001$).
Conclusions: The study concluded that thalassemia as a chronic disease has a negative impact on HRQoL and muscle strength of children in different age group.

1. Introduction

Thalassemia is a genetic blood disorder, which is characterized by decreased synthesis or absence of globin [1]. This synthetic defect leads to the formation of fragile abnormal red blood cells (RBC), which can be easily hemolyzed, leading to chronic anemia [2]. According to clinical and hematological conditions, the severity of the disease is classified into three categories; beta thalassemia carrier state, thalassemia intermedia and thalassemia major [3].

The World Health Organization (WHO) recognized thalassemia as the most prevalent genetic blood disorder in the world, found in more than 60 countries with a carrier population of up to 150 million [4]. This disorder is highly prevalent among children in the Middle East, Mediterranean region, and South Asia [5].

Thalassemia is a chronic disease and presents with a wide range of serious clinical and psychological challenges. The effects of thalassemia on physical health can lead to physical deformity, growth retardation, and delayed puberty [5–7]. Its impact on physical appearance, e.g., bone deformities and short stature, also contributes to a poor self-image [5,7]. Severe complications such as heart failure, cardiac arrhythmia, liver disease, endocrine complications, and infections are common among thalassemia patients [8]. These problems do not only affect patients' physical functioning but also their emotional functioning, social functioning and school functioning, leading to impaired health-related quality of life (HRQoL) of the patients [5,7,9,10].

Children with thalassemia are less active than their healthy peers and generally have decreased muscle strength and flexibility [11]. Pain has become increasingly common and an emergent complication of thalassemia. The exact mechanism of pain in thalassemia has not yet been clarified; however, iron overload, low hemoglobin level, and low bone mass have been suggested as possible causes [12]. Nevertheless, the current evidence does not confirm these suggestions. The most frequent sites of pain were the lower back (82%), the leg (56%), head (48%), and mid-back (47%). [13].

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Health Related Quality of Life studies on children with chronic illness such as thalassemia are limited. The assessment of HRQoL in children, especially in children with chronic illness such as thalassemia is particularly important [14].

1.1. Aim of the study

The aim of this study was to evaluate health related quality of life, muscle strength, and pain in children with β-thalassemia major.

1.2. Methods

1.2.1. Subjects

For the purpose of the study, 120 children ranged in age from 2 to 12 years were enrolled in a cross-sectional study from October 2017 to April 2018. 60 children with β-thalassemia major (32 girls and 28 boys) were selected by a blind physician from the outpatient clinic of "Abo El-Rish Pediatric Hospital – Cairo University Hospitals". In addition, 60 healthy age-matched children with normal hemoglobin level (25 girls and 35 boys) were selected from Abo-Bakr El-Sedik Primary school in Sheikh Zayed City. All selected children were free from musculoskeletal deformities, visual and auditory impairments. However, children who had associated disease with β-thalassemia major as leukemia or marked cognitive or cardiac impairments were excluded from the study. The children either thalassemic or normal were stratified into three age subgroups (I (2–4 years), II (5–7 years) and III (8–12 years). Before the study, interviews were conducted with the children and their parents to explain the purpose, procedures as well as potential benefits of the study and signed a consent form of the ethical committee, Faculty of Physical therapy, Cairo University prior to participation. The study design, protocol and consent forms were carried out in accordance with the code of ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans.

1.2.2. Instrumentation for evaluation

1.2.2.1. Handgrip strength. The handheld dynamometer has been shown to be reliable in measuring hand-grip strength in children [15].Hand-grip strength of the dominent side was measured in pounds using a hand-held dynamometer (Nicholas Manual Muscle Test system, Model 01163; Lafayette Instrument Company, Lafayette, IN).

1.2.2.2. Health related quality of life. Assessment of the HRQoL of children was performed using the pediatric quality of life inventory™ (PedsQL™) 4.0 generic core scale which was developed to measure HRQoL in healthy children and adolescent and those with acute and chronic health problems. PedsQL™ 4.0 is reliable, feasible, and valid to measure the health outcome of the pediatric population, as it facilitates risk assessment and tracking of community health [16]. The Arabic version of PedsQL™ 4.0 was considered to have satisfactory psychometric properties according to a Jordanian study conducted by Arabiat et al. [17]. 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 to be appropriate for ages of the children. In children older than 4 years, it includes parallel child self-reports and parent proxy reports (age ranges 5–7, 8–12 and 13–18 years) and consists of 23 items. Moreover, in children aged between 2 and 4 years, parent proxy report was used and consists of 21 items. The scale was applied, and analyzed according to the PedsQL™ administration guidelines [SM]. The children were asked to report problems regarding physical functioning (8 items), emotional functioning (5 items), social functioning (5 items) and school performance (5 items) that have arisen for the past one month. The items' responses were measured on a five-point rating scale which consists of 0 (never a problem), 1 (almost never a problem), 2 (sometimes a problem), 3 (often a problem), and 4 (almost always a problem), yielding a total score with corresponding scores of 100, 75, 50, 25, and 0. The higher score indicating higher QoL, better health or a higher level of function. 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 [14].

1.2.2.3. Pain. Pain was measured by using the Visual Analogue Scale (VAS), which represents quantitative measurement in terms of a straight line placed horizontally. Both ends of the line are labeled with descriptive terms to anchor the extremes of the scale and to give reference to any point in the continuum between them. The line was 10 cm in length and each cm has its own number that reflected the amount of pain. The VAS is the most common and reliable type of pain scale [18].

1.2.3. Procedures

1.2.3.1. Anthropometric measurements. Weight (kg) and height (m) were recorded using a calibrated floor scale (ZT-120 model), Hangzhou Tianheng Technology Co., Ltd. Hangzhou, China. Body mass index (BMI) was calculated as weight (kg)/height^2 (m).

1.2.3.2. Handgrip strength. The purpose and steps of the procedure were explained to the children and their caregivers. Each child was asked to indicate the dominent hand, any pain at one hand or both, or any kind of injury or surgery that could affect the result of the test. The children were seated in front of a table in an appropriately adjusted chair during measurements. The children sit with the shoulder adducted, the elbow flexed in a 90° angle, and the forearm and wrist in a neutral position. Before the start of each measurement, the child was asked to handle the dynamometer and when ready the child was told, "Squeeze your hand as hard as you can" then release. Three maximum voluntary contractions were recorded for the dominent hand with a rest period of 5 min. The first attempt is used for familiarization, and the score will be obtained by averaging the second and third attempts.

1.2.3.3. Health related quality of life. The PedsQL™ 4.0 generic core scale was explained to all children and their caregivers who were ensured of confidentiality of their information. In the present study, the questionnaires were distributed among the parents of children who filled out the questionnaires in the presence of the investigator. One questionnaire was given to each participant and the investigator completed the questionnaire with respect to ethical principles for those patients who were illiterate.

1.2.4. Statistical analysis

Descriptive statistics in the form of mean, standard deviation and frequencies were conducted for data presentation. *T*-test were conducted for comparison of the subject characteristics between groups. Chi-square test was conducted for comparison of sex distribution and school attendance between both groups. Qol, hand grip strength and VAS were compared between groups using *t* test. The level of significance for all statistical tests was set at $p < 0.05$. All statistical measures were performed through the statistical package for social studies (SPSS) version 19 for windows.

Table 1
Mean age, weight, height and BMI of control and thalassemia group.

	normal group $\bar{X}$ ±SD	Thalassemia group $\bar{X}$ ±SD	t-value	p-value
Age (years)	6.71 ± 2.85	6.5 ± 2.9	0.41	0.68*
Weight (kg)	22.63 ± 9.52	21.75 ± 8.87	0.52	0.6*
Height (cm)	113.36 ± 16.72	110.68 ± 16.28	0.89	0.37*
BMI (kg/m^2)	16.79 ± 2.89	17.05 ± 3.04	−0.49	0.62*
Males/females	35/25	28/32	χ^2 = 1.63	0.2*

$\bar{X}$, Mean; SD, Standard deviation; χ^2, Chi squared value; p value, Probability value; *, significant.

2. Results

2.1. Demographic characteristics of the participants

Sixty children with β-thalassemia major were compared with 30 healthy children. Table 1 showed the mean age, weight, height and BMI of both groups. There was no significant difference between both groups in subject characteristic ($p > 0.05$). In addition, there was no significant difference in sex distribution between groups ($p = 0.2$).

2.2. Clinical characteristics of the thalassemia children

There was a positive family history of thalassemia in 63% of the children. Most children (56.66%) had Hb concentration below 7 g/dl. The age of onset was less than 6 months in 75% of children. Approximately half of the children (53%) received blood transfusion regularly every 2 weeks. Most of the children (60%) had a history of splenectomy. Eighty-three percent of our children were receiving iron-chelation therapy (Table 2).

2.3. School attendance

Fifty-eight (97%) of children in the control group were attending school while 40 (67%) in the thalassemia group were attending school as shown in Table 3. There was a significant decrease in school attendance of the thalassemia group compared with that of the control group ($p = 0.0001$).

Table 2
Clinical characteristics of the thalassemia children.

Clinical data	*n*	*%*
Family history of thalassemia		
Yes	38	63%
No	22	37%
Hb		
<7 g/dL	34	56.66%
7–9 g/dL	25	41.66%
>9 g/dL	1	1.66%
Age of onset		
<6 months	45	75%
6–12 months	9	15%
>12 months	6	10%
History of splenectomy		
Yes	36	60%
No	24	40%
Use of chelation therapy		
Yes	50	83%
No	10	17%
Frequency of transfusion		
Every 2 weeks	32	53%
Every 3 weeks	4	7%
Monthly	16	27%
Every 2 Months	8	13%

Hb, hemoglobin; n, number; %, percentage.

2.4. Health related quality of life (HRQoL)

Children in the thalassemia group demonstrated significant reduction in HRQoL measures when compared with the control group. There was a significant decrease in physical functioning, emotional functioning, social functioning and school functioning of the thalassemia group compared with that of the control group ($p = 0.0001$). School functioning showed the largest difference with the control group (MD = 53.95) followed by physical functioning (MD = 23.31). (Table 4).

2.5. Handgrip strength

There was a significant reduction in handgrip strength of the thalassemia group compared with the control group ($p = 0.0001$).

2.6. Pain

There was a significant increase in VAS score of the thalassemia group compared with control group ($p = 0.0001$).

3. Discussion

The present study assessed the handgrip strength and HRQoL in children with β-thalassemia major. The main findings suggested that children with β-thalassemia major demonstrated lower scores of handgrips strength associated with poor HRQoL in terms of physical, emotional, social and school functioning when compared with the healthy age-matched children.

The results of the present study showed that most of the studied children in the thalassemia group had positive family history, history of splenectomy and use of chelation therapy with a percentage of 63%, 60% and 83% respectively. These results are consistent with the findings of Ayoub et al. [19] who reported the same results in Saudi Arabia in family history (64.4%) and use of chelation therapy (87%). However, the history of splenectomy is different and registered low percentage (34.8%).

Concerning Hb concentration, the Hb level in the thalassemia group is much lower than in the healthy age matched children. These results confirmed those already reported by Galanello and Origa [20] who reported that patients with thalassemia major are characterized by reduced Hb level (<7 g/dl) with reduced RBCs which resulted in microcytic anemia.

In school attendance, the third of the studied children in the thalassemia group (33%) were not attending school. This high percentage means that children with β-thalassemia major were educationally retarded and demonstrated deficiencies in terms of academic achievement. The reasons for this retardation could be explained as the children could not attend school daily due to feeling of fatigue, fear of trauma as well as the need for frequent blood transfusions. These results come in agreement with Pakbaz et al. [21] and Ayoub et al. [19] who reported that thalassemia patients showed decreased academic achievement, which was due to frequent absence from the school for visiting health care centers

Table 3
The frequency distribution and chi squared test for comparison of school attendance between both groups (the control and thalassemia).

	Control group	Thalassemia group	χ^2	p-value	Sig
Attending school	58 (97%)	40 (67%)	18.03	0.0001	S
Not attending school	2 (3%)	20 (33%)			

χ^2, Chi square value; p value, Probability value; S, Significant.

Table 4
Comparison of HRQol, strength and pain between the control and thalassemia group:

	Control group $\bar{X}$ ±SD	Thalassemia group $\bar{X}$ ±SD	MD	t-value	p-value
Physical functioning	85.1 ± 10.23	61.79 ± 18.59	23.31	8.5	0.0001**
Emotional functioning	84.08 ± 9.45	71.08 ± 17.78	13	5	0.0001**
Social functioning	92.5 ± 7.33	73.91 ± 17.99	18.59	7.4	0.0001**
School functioning	85.2 ± 17.62	31.25 ± 25.9	53.95	13.34	0.0001**
Hand grip strength (lb)	1.96 ± 1.14	0.93 ± 0.74	1.03	5.84	0.0001**
Pain (VAS)	0 ± 0	6.28 ± 1.8	−6.28	-26.96	0.0001**

$\bar{X}$, Mean; SD, Standard deviation; MD, Mean difference; p value, Probability value; **, Significant.

and regular blood transfusions, reduced self-confidence, hospitalization as well as physical and mental problems.

The decreased values of handgrip strength in children with thalassemia could be attributed to increased pain in the joints, decreased exercise capacity and physical function in these children. These results corroborate with the findings of Jagoe and Engelen, [22] who reported that the presence of pain that may involve the functional status in patients with thalassemia could result in less muscular work and a consequent change in muscle protein metabolism that can lead to peripheral muscle weakness over time. Decreased handgrip strength in children with thalassemia may be due to the significant long-term consequences of chronic transfusion on nutrition, physical activity, and growth [23]. These results were supported by the findings of Boot et al. [24] who reported that body composition is influenced by many factors including age, gender, gonadal status, nutrition, exercise, and hormonal factors. Moreover, the decreased hemoglobin levels could result in decreased muscular strength in these children, as lower hemoglobin level is associated with a number of symptoms, such as fatigue, general weakness and decreased mental alertness, which may lead to impaired HRQoL [25].

The results of the present study demonstrated that school functioning domain was the most affected domain followed by physical, emotional and social functioning respectively in QoL in children with thalassemia. These results are the same and consistent with the findings of Ayoub et al. [19], Thavorncharoensap et al. [26] and Ismail et al. [27] who reported that school functioning had a lower score followed by physical, emotional and social functioning. This could be explained by the fact that frequent absence from school for hospital visits, and lack of energy when performing academic activities, had a significant negative impact on the children's HRQoL [14,28].

The findings of this study are consistent with the observations of Ismail et al. [14], who investigated the effect of thalassemia on children (age, 5–18 years) compared with healthy children (age, 7–18 years) in terms of physical, emotional, social and school functioning using the PedsQL 4.0 generic scale score. They concluded that thalassemia has a negative impact on all the measured variables in children with thalassemia compared with the healthy controls.

The results of the current study also confirm those already reported by Baraz et al. [29] who compared the QoL between 65 adolescents with beta thalassemia major (age, 14–18 years) and their healthy peers with the same number and age. They concluded that the adolescents with beta thalassemia had lower QoL compared with their healthy age-matched subjects. Similarly, Gharaibeh and Gharaibeh [30] compared the outcomes of PedsQL obtained on a sample of 128 Jordanian thalassemic children aged 8–18 years with those of 83 healthy children. The patients had significantly lower HRQoL mean scores in all dimensions compared to their healthy peers.

Increased pain scores in children with thalassemia could be attributed to low hemoglobin concentration, low bone mass, and/or iron overload. Moreover, as individuals with thalassemia increase in age, pain becomes more common, more severe and the number of sites of pain increase. Pain interferes with multiple dimensions of life, particularly emotional and physical functioning [13].

This is also consistent with Trachtenberg et al. [31] who reported that patients with thalassemia as they age frequently complain of "throbbing back pain" in the week before transfusion. Practitioners generally assumed that bone marrow activity and pressure are increased, which are subsequently suppressed after blood transfusion. This assumption is supported by 34% of patients reported improvement of pain with transfusion. Marrow expansion could also be a source of pain.

Some limitations to this study should be recognized. The relatively small sample size that limit the generalizability of the findings. In addition, lack of previous studies that assessed muscle strength in children with thalassemia that limit the comparison of our data with other studies. There is a need for conducting more research on cardiopulmonary strength and fitness and their relationship with functional and social activity in these children.

4. Conclusion

Thalassemia as a chronic disease has a negative impact on muscle strength, pain and HRQoL in terms of physical functioning, emotional, social and school functioning when compared with the healthy age-matched children. Therefore, intervention programs emphasizing spiritual growth, physical activity and interpersonal relations are necessary for children with thalassemia.

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References

[1] Surapolchai P, Satayasai W, Sinlapamongkolkul P, Udomsubpayakul U. Biopsychosocial predictors of health related quality of life in children with thalassemia in Thammasat University Hospital. J Med Assoc Thai 2010;93(7):65–75.

[2] Baghianimoghadam MH, Sharifirad G, Rahaei Z, Baghianimoghadam B, Heshmati H. Health related quality of life in children with thalassaemia assessed on the basis of SF-20 questionnaire in Yazd, Iran: a case-control study. Cent Eur J Public Health 2011;19:165–9.

[3] Vlychou M, Alexiou E, Thriskos P, Fezoulidis I, Vassiou K. Body composition in adult patients with thalassemia major. Int J Endocrinol 2016;2016:1–7.

[4] Cao A, Galanello R. Effect of consanguinity on screening for thalassemia. N Engl J Med 2002;347(15):1200–2.

[5] Mikelli A, Tsiantis J. Brief report: Depressive symptoms and quality of life in adolescents with thalassaemia. J Adolesc 2004;27:213–6.

[6] De Sanctis V, Roos M, Gasser T, Fortini M, Raiola G, Galati MC. Impact of long-term iron chelation therapy on growth and endocrine functions in thalassaemia. J Pediatr Endocrinol Metab 2006;19:471–80.

[7] Telfer P, Constantinidou G, Andreou P, Christou S, Modell B, Angastiniotis M. Quality of life in thalassemia. Ann N Y Acad Sci 2005;1054:273–82.

[8] Caro JJ, Ward A, Green TC, Huybrechts K, Arana A, Wait S, et al. Impact of thalassemia major on patients and their families. Acta Haematol 2002;107:150–7.

[9] Cao A. Quality of life and survival of patients with betathalassemia major. Haematologica 2004;89:1157–9.

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

[11] Wong DL, George E, Tan MA. A holistic approach to education program in thalassemia population: Consideration of perspectives, attitudes and perceived needs. J. Community Genet 2011;2(2):71–9.

[12] Giardina PJ. Pain in thalassemia - an emerging complication. Thalass Rep. 2011;1:e23.

[13] Haines D, Martin M, Carson S, Oliveros O, Green S, Coates T, et al. Pain in thalassaemia: the effects of age on pain frequency and severity. Br J Haematol 2013;160:680–7.

[14] Ismail A, Campbell MJ, Ibrahim HM, Jones GL. Health Related Quality of Life in Malaysian children with thalassaemia. Health Qual Life Outcomes 2006;4:39.

[15] Molenaar HM, Zuidam JM, Selles RW, Stam HJ, Hovius SE. Age-specific reliability of two grip-strength dynamometers when used by children. J Bone Joint Surg Am 2008;90:1053–9.

[16] Varni JW, Burwinkle TM, Seid M, Skarr D. The PedsQL 4.0 as a pediatric population health measure: feasibility, reliability, and validity. Ambul Pediatr 2003;3:329–41.

[17] Arabiat D, Elliott B, Draper P, Al Jabery M. Cross-cultural validation of the Pediatric Quality of Life Inventory 4.0 (PedsQL) generic core scale into Arabic language. Scand J Caring Sci 2011;25:828–33.

[18] Ferraz MB, Quaresma MR, Aquino LR, Atra E, Tugwell P, Goldsmith CH. Reliability of pain scales in the assessment of literate and illiterate patients with rheumatoid arthritis. J Rheumatol 1990;17(8):1022–4.

[19] Ayoub MD, Radi SA, Azab AM, Abulaban AA, Balkhoyor AH, Bedair SW, et al. Quality of life among children with beta-thalassemia major treated in Western Saudi Arabia. Saudi Med J 2013;34(12):1281–6.

[20] Galanello R, Origa R. β-thalassemia. Orphanet J Rare Dis 2010;5:11.

[21] Pakbaz Z, Treadwell M, Yamashita R, Quirolo K, Foote D, Quill L, et al. Quality of life in patients with thalassemia intermedia compared to thalassemia major. Ann N Y Acad Sci 2005;1054:457–61.

[22] Jagoe RT, Engelen MP. Muscle wasting and changes in muscle protein metabolism in chronic obstructive pulmonary disease. Eur Respir J Suppl 2003;46:52–63.

[23] Fung EB, Xu Y, Kwiatkowski JL, Vogiatzi MG, Neufeld E, Olivieri N, et al. Relationship between chronic transfusion therapy and body composition in subjects with thalassemia. J Pediatr 2010;157:641–7.

[24] Boot AM, Bouquet J, de Ridder MA, Krenning EP, de Muinck Keizer-Schrama SM. Determinants of body composition measured by dual-energy x-ray absorptiometry in Dutch children and adolescents. Am J Clin Nutr 1997;66:232–8.

[25] Shumaker S, Berzon R. The International Assessment of HROL: Theory, Translations, Measurement and Analysis. Oxford: Rapid Communications; 1995.

[26] Thavorncharoensap M, Torcharus K, Nuchprayoon I, Riewpaiboon A, Indaratna K, Ubol BO. Factors affecting health-related quality of life in Thai children with thalassemia. BMC Blood Discord 2010;10(1):1.

[27] Ismail M, Chun C, Yusoff N, Shahar S, Abdulmanaf Z, Rajikan R, et al. Quality of life among thalassaemia children, adolescent and their caregivers. Sains Malaysiana 2013;42(3):373–80.

[28] Musallam K, Cappellini MD, Taher A. Challenges associated with prolonged survival of patients with thalassemia: transitioning from childhood to adulthood. Pediatrics 2008;121(5):1426–9.

[29] Baraz S, Miladinia M, Mosavinouri E. A comparison of quality of life between adolescences with beta thalassemia major and their healthy peers. Int J Pediatr 2016;4:1195–204.

[30] Gharaibeh HF, Gharaibeh MK. Factors influencing health-related quality of life of thalassaemic Jordanian children. Child Care Health Dev 2012;38(2):211–8.

[31] Trachtenberg F, Foote D, Martin M, Carson S, Coates T, Beams O, et al. Pain as an emergent issue in thalassemia. Am J Hematol 2010;85:367–70.