ORIGINAL ARTICLE

QUALITY OF LIFE AND ITS DETERMINANTS IN TRANSFUSION DEPENDENT THALASSEMIA

Asfandyar Roghani, Naseem Khan*, Inayat Shah*, Saba Khan, Abid Sohail Taj*, Yasar Mehmood Yousafzai***

Pak International Medical College, Peshawar, Pakistan, *Institute of Basic Medical Sciences, Khyber Medical University, **Hayatabad Medical Complex, Peshawar, Pakistan

Background: Patients with transfusion-dependent Beta-Thalassemia carry the burden of chronic illness throughout their lives. Data regarding the impact of disease on the quality of life of these patients is scant. The objective of this study was to assess physical and emotional aspects, family health, school & career functions, and overall quality of life of children with transfusion-dependent thalassemia major and to investigate the determinants of quality of life. **Methodology:** A total of 365 patients registered in selected thalassemia centres of Peshawar, participated in the study. Data regarding effect of thalassemia on mental health, physical health, family life, career and school was collected using the TranQol questionnaire. Additionally, in a subset of patients (n=40) clinical and molecular genetic information were also collected to assess the role of these variables as determinants of quality of life. **Results:** Study revealed that thalassemia major affects quality of life negatively. The disease has its manifestations on physical (mean effect 36.05±13.80), emotional (mean effect 42.10±9.42) and family health (mean effect 55.44±8.85) as well as school and career (mean effect 25.85±15.69) of the patients. Moreover, The TranQol scores were positively correlated with higher Hb and hydroxyurea therapy and negatively correlated with serum ferritin levels of patients. **Conclusion:** Physical, emotional, family and school health are all negatively affected by the transfusion dependent thalassemia. Quality of Life is directly proportional to the Hb levels and use of Hydroxyurea therapy, and inversely proportional to levels of ferritin.

Keywords: Thalassemia, Transfusion, Quality of Life, TranQol

Pak J Physiol 2018;14(3):64–7

INTRODUCTION

Beta thalassemia is one of the commonest genetic disorders in Pakistan. An estimated 80–90 thousand children are currently affected by transfusion-dependant thalassaemia.[1] Significant improvements have been made in previous decades in developed countries and overall survival at 25 years is >90% and at 50 years is >70%.[2] Regular blood transfusions, iron chelation and bone marrow transplantation have contributed to increased life expectancy. Recent introduction of hydroxyurea for Haemoglobin F augmentation has further reduced the frequency of blood transfusions and its related complications.[3] Yet significant challenges remain. Firstly, quality blood transfusion services are not available in majority of districts in Pakistan. Inadequate screening of blood products has resulted in unacceptable levels of Transfusion Transmitted Infections (TTIs). The reported incidence of TTIs in Transfusion-dependant thalassemia children is as high as 25%.[4] In addition; blood transfusion is provided on replacement basis, i.e., patients have to arrange a blood donor for each transfusion they receive in the hospitals.[5] This adds to the financial and social burden on the patients and their families.[6] Secondly, regular transfusions rapidly lead to iron overload. Most published literature from Pakistan has reported inadequate iron chelation evident by very high levels of serum ferritin in thalassemia patients.[7,8] Deferoxamine treatment regimen is difficult to administer whereas Deferasirox is beyond the affordability of most patients. Thirdly, bone marrow transplant is only offered by a handful of centres in Pakistan and most patients cannot afford this expensive procedure.[9,10] All these challenges increase the physical, emotional and social burden on patients, their families and the society.

The aim of management of thalassemia is not only to treat the disease, but also to improve quality of life (QoL) of patients and help patients become productive members of the society. A number of tools have been designed to measure the effect of disease on quality of life of patients. Published reports using Health Related Quality of Life (HR-QoL), Short-Form 36 (SF-36) and Paediatric Quality of Life (PedsQoL) questionnaires show transfusion-dependant thalassemia significantly impairs QoL of patients.[11–13] However; these tools are not disease specific. More recently, a new disease specific quality of life tool; transfusion dependent quality of life (TranQol) questionnaire was developed to precisely determine the QoL in transfusion-dependant Thalassemia patients.[14,15] This self-reported questionnaire comprises physical, mental, family support, social and school functioning domains.

Data on overall survival of Pakistani thalassemic children is scant[16], however, it claims some

improvement in life expectancy.[17] Whether this improvement has translated into better physical, mental and social functioning of patients is not known. Various factors that affect QoL in Pakistani thalassemia patients have never been investigated. The aim of this study was to determine the QoL of transfusion-dependant thalassemia patients in three transfusion centres of Peshawar. As a secondary aim, we tested association of clinical and laboratory parameters like age, sex, Hb levels, treatment modality, serum ferritin levels and Xmn1 polymorphism with TranQol score.

MATERIAL AND METHODS

This cross sectional analytical study was conducted after getting approval from Ethical Review Board of Khyber Medical University, Peshawar. Written informed consent was also obtained from all the patients or their parents.

Sample size was calculated using WHO sample size calculator. Considering the values of alpha as 95%, population mean as 55, population standard deviation as 7 and absolute precision as 0.72, a sample size of 360 was calculated, however, we included 365 patients in the current study.

Transfusion-dependent thalassemia patients treated in three blood transfusion centres of Peshawar (Fatimid Foundation, Frontier Foundation and Hayatabad Medical Complex were recruited from February 2015 to February 2016. All patients aged 8 and above and diagnosed as thalassemia with haemoglobin electrophoresis were included in the study. Patients requiring fewer than 6 transfusions per year and with co-morbidities unrelated to thalassemia were excluded.

Quality of life was measured using TranQol questionnaire.[14] This is a specific QoL questionnaire for patients with thalassemia requiring regular transfusion. TranQol assesses patients' QoL in four domains: physical health, mental health, family health, and career and school function, and comprise 28 questions. This is a self-administered tool with written instructions. The responses are recorded as one of the five options: 'never', 'almost never', 'sometimes', 'often', and 'always' and coded as 1 to 5 respectively. The questionnaire bears high reliability and construct validity.[15] The minimum score for all variable questions on tranQol is 28 and maximum score is 140. Reverse coding was done for negatively phrased questions. In the current study, an interviewer assisted the patients and translated items for the patients with limited literacy ability. In a subset of patients (n=40) additional clinical information including demographic variables, presence of hepatosplenomegaly, Haemoglobin levels, serum ferritin levels, presence or absence of Xmn1 polymorphism and hydroxyurea therapy were noted.

Data was analysed using SPSS-23. Mean and standard deviation were calculated for quantitative variables whereas frequency and percentage for qualitative variables. Multivariable analysis of the TranQol was carried out whereby mean and standard deviation of each variable (item analysis) and that of individual domains (domain analysis) were calculated. The mean score of each domain was converted to percentage for the purpose of comparison between different domains. To find out association between TranQol and different clinical parameters the quantitative variables were converted to categorical variables and Chi Square test was applied to find out association. Alpha value was kept at 0.05 for the control of alpha error.

RESULTS

Out of 365 participants, 212 (58.1%) were males and 153 (41.9%) were females. Mean age of participants was 11.9±3.13 years with 240 patients (65.8%) below 12 years of age, and 125 (34.2%) above 12 years.

Clinical, demographic and genetic information from a subset of patients (n=40) were also collected. The associations of Quality of Life Scores with clinical features given in Table-1 were analyzed. Patients were divided into high (good) QoL score >50 and low (poor) score <50 and the demographic and clinical parameters were compared between the two groups. A statistically significant positive correlation with increased haemoglobin (p=0.01), low ferritin level (p=0.03) and hydroxyurea treatment (p=0.02) was noted. On the other hand, there was statistically non-significant association of QoL with age, gender, hepatomegaly, splenomegaly and Xmn-1 polymorphism.

Table-2 shows item and domain analysis of the questionnaire. It also shows composite analysis of the total questionnaire. For comparison between different domains, the mean scores are also presented as percentage.

Table-1: Association of demographic, clinical and genetic parameters with QoL

Clinical features		Score >50 N=20 [n (%)]	Score <49 N=20 [n (%)]	p
Hb (g/dl)	>6	12 (85.7)	2 (14.3)	0.01*
	<6	8 (30.8)	18 (69.2)	
Ferritin (ηg/ml)	<2000	17 (68)	8 (32)	0.03*
	>2000	3 (20)	12 (80)	
Age (Years)	8–17	18 (90)	18 (90)	1.00
	18–26	2 (10)	2 (10)	
Gender	Male	14 (48.3)	15 (51.7)	0.72
	Female	6 (54.5)	5 (45.5)	
Hepatomegaly	Yes	6 (46.2)	7 (53.8)	0.73
	No	14 (51.9)	13 (48.1)	
Splenomegaly	Yes	13 (46.4)	15 (53.6)	0.49
	No	7 (58.3)	5 (41.7)	
Xmn1 polymorphism	Yes	6 (100)	0 (0)	0.08
	No	14 (41.2)	20 (58.8)	
Hydroxyurea treatment	Yes	15 (75)	5 (25)	0.02*
	No	5 (25)	15 (75)	

Table-2: Item, domain and overall analysis of TranQol questionnaire

Domain	Variable	Mean±SD	Domain Mean±SD	Percent score
Physical Health	1. Difficulty Sleeping	1.71±0.71	10.81±4.07	36.05±13.60
	2. Pain and discomfort	1.43±0.91		
	3. Pain prevent from work	1.84±0.46		
	4. Felt tired	1.86±0.58		
	5. Difficulty Playing	1.93±0.49		
	6. Social activities	2.04±0.92		
Emotional Health	7. Worried from lab tests	2.40±0.45	18.94±4.24	42.10±9.42
	8. Felt different	3.12±0.37		
	9. Worried disclosing disease	1.93±0.50		
	10. Worried about prognosis	1.63±0.48		
	11. Worried getting infections	2.84±0.38		
	12. Felt angry	1.54±0.59		
	13. Felt Sad	1.46±0.43		
	14. Treatment prevent from work	2.37±0.45		
	15. Patient put off transfusion	1.65±0.59		
Family Health	16. Family support	3.73±0.29	24.94±3.91	55.44 8.85
	17. Friends support	3.61±0.37		
	18. Disease affects family	1.85±0.63		
	19. Taking decision in treatment	2.51±0.43		
	20. Fought with parents for treatment	2.91±0.53		
	21. Parents didn't allow for work	2.33±0.48		
	22. Child included in decision	3.43±0.34		
	23. Child liked to be included in decision	3.24±0.39		
	24. Child thought Thalassemia treatment caused shortage of money	1.33±0.45		
School and career	25. Thalassemia affected school life	1.10±0.63	5.17±3.13	25.85±15.69
	26. Thalassemia affected school work	1.07±0.52		
	27. Had trouble keeping up with school work	1.14±0.74		
	28. Child was bothered missing school	1.86±1.24		
Total score			59.86±15.35	42.77±7.60

*Significant

DISCUSSION

This study aimed to measure emotional, physical and social life aspects and overall QoL scores for thalassemia patients in Peshawar, Pakistan and to determine the clinical and genetic factors associated with QoL scores. The results show that patients reported poor quality of life in all the domains of TranQol questionnaire.

Our study reported that Pakistani transfusion-dependent thalassemia children have significantly poor physical quality of life compared to international[15] and regional cohorts.[11-13,18] There has only been one study using Transfusion-specific quality of life questionnaire (TranQol) with reported mean physical health scores of 79.6.[14,15] The differences in perceived physical health may be due to a multitude of reasons. Majority of our patients do not receive regular transfusions or iron chelation. Consequently, patients develop hepatosplenomegaly, severe anaemia and iron overload. Hepatosplenomegaly increases intra-abdominal pressure and the physical activity in patients with hepatosplenomegaly induces pain and discomfort. Further restriction of physical activity is caused by anaemia which induces breathlessness and palpitations with playground activities. Bone marrow expansion and bone loss causes bone pains and further limit the child's ability to play sports. In addition, many patients receive Deferoxamine which further limits their mobility during the day. This is evident by high TranQol scores for patients with higher Hb and low serum ferritin levels. Furthermore, patients on Hydroxyurea had a significantly higher QoL score as compared to patients treated with transfusions alone. In our thalassemia centres, transfusions and Deferoxamine chelation are given during working hours which limit the patients' school attendance and play time. Taken together, these findings suggest that patients who were better transfused and chelated or who received fewer transfusions due to hydroxyurea had better quality of life.

The scores in emotional health were found to be poor in comparison with international studies[11-13,15,18] although differences were smaller than those of physical health scores. Mental health is affected by physical, societal, and financial factors. Personal relations, participation in social activities and leisure time may be affected by the burden of chronic illness and life-long treatment.[19] Since children are treated in thalassemia treatment centres where other patients with various complications are also treated, they felt worried about their prognosis and getting infections from transfusions. Chronic pain might further deteriorate the mental health of patients.

Our study reports negative effect of transfusion-dependent thalassemia on the family health scores of patients. In comparison to mean scores of 55.5 in our children, Klaassen *et al* reported scores of 77.8 in the Canadian cohort. However, studies from Egypt[12] and India[11] reported comparable scores of 59.6 and 60.1 respectively. These relatively higher scores in family health domain reflect emotional and financial support from family. In absence of an effective state-sponsored healthcare, and with many patients living in joint families, the family provides financial, logistic and

emotional support for treatment.[20] On the other hand, school and career functioning scores were lowest in our patients. Thalassemia children go to regular schools where other children and staff are not trained for dealing with children with disabilities and chronic illnesses. Both disease and its treatment affect school attendance, grades and play time. Although there are currently no requirements of special education for thalassemic children, however, for poorly treated children, attending regular schools can be challenging.

Patients with transfusion dependent thalassemia have substantially low self-perceived quality of life in physical, emotional, family and school domains. The TranQol scores are higher in well-managed patients with high Hb and low ferritin, or patients treated on Hydroxyurea. This study has a number of limitations: first, clinical and genetic data was not collected for all 365 patients. Secondly, as TranQol is transfusion-specific questionnaire, no healthy control group could be included in the study. Thirdly, no private transfusion centres were included. Private patients might receive better care and might score higher on the questionnaire. Despite these weaknesses, this is the first study in Pakistan to investigate quality of life in transfusion-dependent thalassemia children. Being a multi-centre study, this represents a larger cross-section of the society.

CONCLUSION

Physical, emotional, family and school health are all negatively affected by the transfusion dependent thalassemia. Quality of Life is directly proportional to the Hb levels and use of Hydroxyurea therapy, and inversely proportional to levels of ferritin. Patients treated on conventional treatment regimen have poor QoL. Any thalassemia treatment protocol should consider the emotional, educational and family support needs of the patients.

REFERENCES

1. Ansari SH, Shamsi TS, Ashraf M, Farzana T, Bohray M, Perveen K, *et al*. Molecular epidemiology of β-thalassemia in Pakistan: Far reaching implications. Indian J Hum Genet 2012;18(2):193–7.
2. Angela V, Giuseppina C, Eliana L, Grazia C, Alessandra Q, Calogera G, *et al*. The era of comparable life expectancy between thalassaemia major and intermedia: Is it time to revisit the major-intermedia dichotomy? Br J Haematol 2017;176(1):124–30.
3. Ansari SH, Shamsi TS, Siddiqui FJ, Irfan M, Perveen K, Farzana T, *et al*. Efficacy of hydroxyurea (HU) in reduction of pack red cell (PRC) transfusion requirement among children having beta-thalassemia major: Karachi HU trial (KHUT). J Pediatr Hematol Oncol 2007;29(11):743–6.
4. Ahmed Kiani R, Anwar M, Waheed U, Asad MJ, Abbasi S, Abbas Zaheer H. Epidemiology of Transfusion Transmitted Infection among Patients with β-Thalassaemia Major in Pakistan. J Blood Transfus 2016;2016:5.
5. Zaheer HA, Waheed U. Blood safety system reforms in Pakistan. J Blood Transfus 2014;12(4):452–7.
6. Shamsi T, Ansari S. Medical management of beta-thalassaemia without blood transfusion: a myth or a reality? J Pak Med Assoc 2013;63(3):304–5.
7. Ejaz MS, Baloch S, Arif F. Efficacy and adverse effects of oral chelating therapy (deferasirox) in multi-transfused Pakistani children with β-thalassemia major. Pak J Med Sci 2015;31(3):621–5.
8. Riaz H, Riaz T, Khan MU, Aziz S, Ullah F, Rehman A, *et al*. Serum ferritin levels, socio-demographic factors and desferrioxamine therapy in multi-transfused thalassemia major patients at a government tertiary care hospital of Karachi, Pakistan. BMC Res Notes 2011;4(1):287.
9. Ali N, Adil SN, Shaikh MU, Masood N. Frequency and Outcome of Graft versus Host Disease after Stem Cell Transplantation: A Six-Year Experience from a Tertiary Care Center in Pakistan. ISRN Hematol 2013;2013:232519 (6 pages).
10. Aljurf M, Zaidi SZ, El Solh H, Hussain F, Ghavamzadeh A, Mahmoud HK, *et al*. Special Issues Related to Hematopoietic Stem Cell Transplantation in the Eastern Mediterranean Region and the First Regional Activity Report. Bone Marrow Transplant 2009;43(1):1–12.
11. Dhirar N, Khandekar J, Bachani D, Mahto D. Thalassemia Major: how do we improve quality of life? Springer Plus 2016;5(1):1895.
12. Elalfy MS, Farid MN, Labib JH, RezkAllah HK. Quality of life of Egyptian b-thalassemia major children and adolescents. Egypt J Haematol 2014;39(4):222.
13. Jafari-Shakib A, Davoudi-Kiakalaye A, Pour-Fathollah A, Jafari-Shakib R, Mohtasham-Amiri Z. Health-Related Quality of Life in β Thalassemia Major Children in North of Iran. Iran J Blood Canc 2016;8(4):108–11.
14. Klaassen R, Alibhai S, Kirby Allen M, Moreau K, Merelles-Pulcini M, Forgie M, *et al*. Introducing the TranQol: a new disease-specific quality of life measure for children and adults with thalassemia major. J Blood Disord Transfus 2013;4.
15. Klaassen RJ, Barrowman N, Merelles-Pulcini M, Vichinsky EP, Sweeters N, Kirby-Allen M, *et al*. Validation and reliability of a disease-specific quality of life measure (the TranQol) in adults and children with thalassaemia major. Br J Haematol 2014;164(3):431–7.
16. Abdul Nasir J, Zaidi SA. Modelling survival data of thalassaemia patients in Pakistan. Journal of Ayub Medical College, Abbottabad: J Ayub Med Coll Abbottabad 2009;21(1):142–5.
17. Riaz H, Riaz T, Khan MU, Aziz S, Ullah F, Rehman A, *et al*. Serum ferritin levels, socio-demographic factors and desferrioxamine therapy in multi-transfused thalassemia major patients at a government tertiary care hospital of Karachi, Pakistan. BMC Res Notes 2011;4(1):287.
18. Ansari S, Baghersalimi A, Azarkeivan A, Nojomi M, Rad AH. Quality of life in patients with thalassemia major. Iran J Ped Hematol Oncol 2014;4(2):57.
19. Turner J, Kelly B. Emotional dimensions of chronic disease. West J Med 2000;172(2):124–8.
20. Improving Chronic Illness Care: Translating Evidence into Action. Health Aff 2001;20(6):64–78.

Address for Correspondence:
Dr Yasar Mehmood Yousafzai, Assistant Professor, Institute of Basic Medical Science, Khyber Medical University Peshawar, Pakistan. **Cell:** +92-321-9054010
Email: yasar.yousafzai@kmu.edu.pk

Received: 16 Mar 2018 Reviewed: 13 Jul 2018 Accepted: 22 Jul 2018