Maternal knowledge on curative therapies and its impact on medical care and psychological health among children with thalassaemia in Sri Lanka

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Abstract

Background: β-thalassaemia is an inherited disorder of haemoglobin synthesis which results in severe transfusion-dependent anaemia from infancy. Although considered a life-limiting disease, it can be cured by allogeneic haematopoietic stem cell transplantation and gene therapy. However, many patients and their families in developing countries are unaware of these treatment options.

Objectives: To assess the maternal knowledge on curative therapies and to determine its association with the adequacy of current medical treatment and psychological health among children with β-thalassaemia.

Method: We conducted a cross-sectional study at the three largest thalassaemia centres of Sri Lanka. All patients with transfusion-dependent β-thalassaemia aged 2-18 years were eligible for the study. Data were collected using an interviewer-administered questionnaire by interviewing mothers and from medical records. The questionnaire contained questions to gather information on socio-demographic background, clinical details and maternal knowledge on curative therapies for thalassaemia. The psychological morbidity of children was assessed using the previously validated 'strengths and difficulties questionnaire'. Binary logistic regression was used in the analysis.

Results: A total of 304 patients (mean age 9.8years; females 54%) were recruited. A majority (86%) of mothers knew that β-thalassaemia can be cured by haematopoietic stem cell transplantation; however, only 1% were aware of gene therapy. Detailed knowledge on curative therapies was lacking in most mothers; only 22% could identify suitable donors for transplantation. Maternal knowledge on curative therapies was associated with higher educational level and income of parents. Accurate maternal knowledge on haematopoietic stem cell transplantation was significantly associated with lower rates of hepatomegaly, splenomegaly, emotional symptoms, conduct symptoms, hyperactive symptoms and abnormal peer relationships in patients.

Conclusions: This study demonstrated that maternal knowledge on curative therapies among patients with β-thalassaemia is sub-optimal. It further demonstrated that having an accurate maternal knowledge is associated with improved medical care and a lower prevalence of psychological symptoms among patients.

(Keywords: Bone marrow transplantation, Haematopoietic stem cell transplantations, Thalassaemia, Psychological health)

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Background

β-thalassaemia is an inherited disorder of haemoglobin synthesis which is characterised by profound anaemia in affected individuals[1,2]. All patients with severe disease require regular blood transfusions from late infancy and remain transfusion-dependent for life[3]. Despite regular transfusions, most patients with β-thalassaemia living in low- and middle-income countries experience a poor quality of life and die prematurely during the fourth or fifth decade[4]. Allogeneic Haematopoietic Stem Cell Transplantation (HSCT) is available as a cure for β-thalassaemia since early 1980s[5]. Thus far, over 3000 patients have been cured by this procedure worldwide[6]. However, the usefulness of allogeneic HSCT has been limited by its cost, lack of suitable donors and the risk of graft versus host disease[7]. Despite this, it is considered as

the first-line treatment for patients with Transfusion-Dependent Beta-Thalassaemia (TDBT) who have Human Leucocyte Antigen (HLA) matched-sibling donors[8]. Gene therapy has emerged as a cure for β-thalassaemia during recent years[9]. A large clinical trial that involved 22 patients who were successfully treated by gene therapy was published recently[10]. Additionally, several promising new genome editing approaches that aim to correct the β-globin mutation, upregulate γ-globin production or down-regulate α-globin synthesis have entered clinical trials or are in late-stage preclinical studies[11-16]. It is likely that these therapies will supplement HSCT to provide a permanent cure for patients with β-thalassaemia in the future.

Sri Lanka is a low-middle income country in South Asia with a population of 22 million. Being in a thalassaemia high prevalent tropical region, the gene frequency of β-thalassaemia in Sri Lanka is reported as 2.8%[17]. Consequently, there are approximately 1800 patients with TDBT receiving supportive treatment in the country[18]. HSCT transplantation for β-thalassaemia was commenced in Sri Lanka in 2014; however, it is available only at a limited number of centres[19]. Due to the limitations in availability and cost, HSCT is not routinely considered as a treatment option for patients with TDBT in many developing countries[20]. This is despite some of them having suitable donors. With the recent advances in HSCT and gene therapy, it is important that all patients with β-thalassaemia and their parents have accurate knowledge on the availability, process, complications, and cost of curative therapies. Also, this knowledge will aid parents to understand the disease and its prognosis better and facilitate making informed decisions. Similarly, it could have a positive impact on adherence to current treatment regimens and the quality of life.

Objectives

To assess the maternal knowledge on curative therapies and to determine its association with the adequacy of current medical treatment and psychological health of children with β-thalassaemia.

Method

We conducted a cross-sectional study at the three largest thalassaemia centres of Sri Lanka located in Kurunegala, Anuradhapura and Ragama Teaching Hospitals. All patients with TDBT aged 2 to 18 years attending these centres from January to March 2018 were eligible to participate in study. Diagnosis of β-thalassaemia was based on the haemoglobin subtype quantification, and transfusion dependency was defined as requiring blood transfusions more frequently than 6-weekly. This group represented over 60% of paediatric patients with TDBT in Sri Lanka. Children attending without their mothers were excluded.

Data were collected using an interviewer-administered questionnaire by interviewing mothers and going through medical records. First section of the questionnaire contained questions on socio-demographic background, blood transfusion history, presence of hepatomegaly or splenomegaly, average pre-transfusion haemoglobin and iron overload status. Second section of the questionnaire contained questions to assess maternal knowledge on curative treatment options for thalassaemia. These included questions to assess mother's awareness of HSCT and gene therapy as a cure for β-thalassaemia and detailed knowledge on HSCT, for example, most suitable donor, cost and complications of HSCT. Final section of the questionnaire contained the previously validated Strengths and Difficulties Questionnaire, which measured the psychological health of children in five domains; emotional, conduct, hyperactivity, peer relationships and pro-social behaviour[21].

Sufficiency of supportive medical treatment was determined by the adequacy of blood transfusions and the iron overload status. Adequate transfusion therapy was demonstrated by pre-transfusion haemoglobin greater than 9g/dL and absence of hepatomegaly and splenomegaly. A serum ferritin value below 1000ng/mL indicated adequate iron chelation[22]. 'Accurate knowledge on HSCT' was defined as precisely knowing the most suitable donor for HSCT.

Ethical Issues: Study was conducted in accordance with the regulations of the Declaration of Helsinki, and ethical approval was obtained from the Ethics Review Committee of the University of Kelaniya, Sri Lanka (No. P/178/07/2017). Mothers of all eligible patients were briefed about the study, and informed written consent from mothers and assent from children over 12 years were obtained before recruiting into the study.

Statistical analysis: Data were analysed using IBM SPSS statistics 22.0 for Windows. Categorical data were expressed as frequencies and percentages. Binary logistic regression was used to determine associations between categorical variables, and both unadjusted and adjusted odds ratios were presented. Cut-off for statistical significance was set at $p<0.05$.

Results

Three hundred and four children with β-thalassaemia were recruited. Mean age was 9.8 ± 4.1 years. Clinical characteristics of study population are shown in Table 1.

Table 2 shows the maternal knowledge on the curative therapies for thalassaemia.

Table 3 shows the determinants of maternal knowledge on curative therapies for thalassaemia. Age, sex, or type of thalassaemia of the child did not have a significant association with the maternal knowledge on a cure for thalassaemia. However, maternal knowledge on a cure was significantly associated with a higher education level of the mother and father. Similarly, a greater proportion of mothers from families with a high monthly income knew that thalassaemia has a cure compared to mothers from lower-income families.

Table 4 shows the association between maternal knowledge on curative therapies and adequacy of medical treatment. There was no significant association between mother knowing about a cure for thalassaemia and adequacy of current medical treatment. However, a significantly lower proportion of children of mothers with an 'accurate knowledge on HSCT' as defined by accurately knowing the best donor for HSCT had hepatomegaly and splenomegaly. Finally, we hypothesised that an improved maternal knowledge on curative therapies for thalassaemia might have a favourable impact on the psychological health among patients.

Table 5 shows the association between maternal knowledge on curative therapies and the psychological health of their children. This revealed that children of mothers who knew about a cure for thalassaemia had a significantly lower prevalence of emotional symptoms ($p<0.05$) and abnormal peer relationships ($p<0.05$). Similarly, 'accurate knowledge on HSCT' in mothers was significantly associated with a lower rate of emotional symptoms ($p<0.01$), conduct symptoms ($p<0.01$), hyperactive symptoms ($p<0.01$) and abnormal peer relationships ($p<0.05$) among children

Table 1

Clinical characteristics of children with thalassaemia (n=304)

Characteristic	n (%)
Type of thalassaemia	
β-Thalassaemia major	255 (83.9)
Haemoglobin E β-thalassaemia	46 (15.1)
Other	03 (01.0)
Sex	
Male	139 (45.7)
Female	165 (54.3)
Age group	
2 – 4 years	40 (13.2)
5 – 12 years	183 (60.2)
13 – 18 years	81 (26.6)
Average pre-transfusion Hb	
< 9g/dL	185 (60.8)
≥ 9g/dL	119 (39.1)
Liver status	
No hepatomegaly	210 (69.1)
Hepatomegaly	94 (30.9)
Spleen status	
No splenomegaly	199 (65.5)
Splenomegaly	98 (32.3)
Splenectomised	07 (02.3)
*Serum ferritin**	
≤ 1000ng/mL	97 (31.9)
>1000ng/mL	196 (64.5)
Psychological symptoms	
Emotional symptoms	55 (18.1)
Conduct symptoms	57 (18.8)
Hyperactivity symptoms	29 (09.5)
Abnormal peer relationships	45 (14.8)
Abnormal social behaviour	08 (02.6)

** Data missing from 11 subjects; Hb: haemoglobin*

Table 2: ***Maternal knowledge on curative therapies for β-thalassaemia (n=304)***

Characteristic	Frequency (%)
Knowledge on curative therapies for thalassaemia	
Knew that thalassaemia has a cure	263 (86.5)
Knew that HSCT is a cure for thalassaemia	262 (86.2)
Knew that gene therapy is an experimental cure	03 (01.0)
Detailed knowledge of HSCT	
Accurately knew the cost of HSCT	62 (20.4)
Accurately knew the best donor for HSCT	69 (22.7)
Knew parents can donate HSC	273 (88.8)
Knew HLA-matched non-relatives can donate HSC	138 (45.4)
Knew cord blood can be a source of HSC	01 (0.3)
Knew graft failure is a complication of HSCT	45 (14.8)
Knew HSCT has an associated mortality	33 (10.9)
Consideration of HSCT as a cure for their child	
Medical staff has discussed HSCT	254 (83.6)
Child has been offered a chance for evaluation for HSCT	177 (58.2)
HLA typing has been done	80 (26.3)
Child is awaiting HSCT	11 (03.6)

HSCT: Haematopoietic stem cell transplantation, HSC: Haematopoietic stem cells, HLA: Human leucocyte antigen

Table 3: ***Determinants of maternal knowledge on curative therapies for thalassaemia***

Characteristic	Mothers knowing thalassaemia has a cure n (%)	Mothers not knowing thalassaemia has a cure n (%)	Unadjusted odds ratio (95%CI)	Adjusted odds ratio (95%CI	p-value
Sex of the child					
Male (n=139)	118 (84.9)	21 (15.1)	0.77	0.79	0.48
Female (n=165)	145 (87.9)	20 (12.1)	(0.40-1.49)	(0.40-1.53)	
Type of thalassaemia					
Thalassaemia major (n=255)	221 (86.7)	34 (13.3)	1.08	1.04	0.93
HbE thalassaemia and other (n=49)	42 (85.7)	07 (14.3)	(0.45-2.60)	(0.43-2.51)	
Mother's educational level					
Above grade 10 (n=99)	92 (92.9)	07 (07.1)	2.61	2.60	<0.05
Grade 10 or below (n=205)	171 (83.4)	34 (16.6)	(1.11-6.12)	(1.10-6.11)	
Father's educational level					
Above grade 10 (n=78)	75 (96.2)	03 (03.8)	5.05	5.04	<0.01
Grade 10 or below (n=226)	188 (83.2)	38 (16.8)	(1.51-16.8)	(1.50-16.8)	
Mother's occupation					
Employed (n=44)	39 (88.6)	05 (11.4)	1.25	1.29	0.60
Unemployed (n=260)	224 (86.2)	36 (13.8)	(0.46-3.39)	(0.47-3.54)	
Father's occupation					
Skilled or professional (n=99)	91 (91.9)	08 (08.1)	2.18	2.16	0.06
Unskilled (n=205)	172 (83.9)	33 (16.1)	(0.96-4.92)	(0.95-4.89)	
Monthly family income					
> LKR 25000 (n=101)	93 (92.1)	08 (07.9)	2.27	2.31	<0.05
≤ LKR 25000 (n=202)	169 (83.7)	33 (16.3)	(1.00-5.11)	(1.01-5.25)	

LKR: Sri Lankan rupees, CI: confidence interval

Table 4: ***Association between maternal knowledge on curative therapies and adequacy of medical care***

Maternal knowledge	Sub-optimal pre-transfusion Hb <9g/dL (n=185)	Optimal pre-transfusion Hb ≥9g/dL (n=119)	Unadjusted odds ratio (95%CI)	Adjusted odds ratio (95%CI)	p- value
Knew about a cure for thalassaemia n (%)	160 (86.5)	103 (86.6)	0.99 (0.50-1.95)	0.96 (0.47-1.96)	0.91
Accurate knowledge on HSCT n (%)	47 (25.4)	22 (18.5)	1.50 (0.85-2.65)	1.54 (0.86-2.76)	0.14
	Hepatomegaly (n=94)	**No hepatomegaly (n=210)**			
Knew about a cure for thalassaemia n (%)	81 (86.2)	182 (86.7)	0.95 (0.47-1.94)	1.50 (0.69-3.22)	0.29
Accurate knowledge on HSCT n (%)	10 (10.6)	59 (28.1)	0.30 (0.14-0.62)	0.30 (0.14-0.64)	<0.01
	Splenomegaly (n=98	**No splenomegaly (n=206)**			
Knew about a cure for thalassaemia n (%)	84 (85.7)	179 (86.9)	0.90 (0.45-1.81)	1.45 (0.69-3.08)	0.32
Accurate knowledge on HSCT n (%)	07 (07.1)	62 (30.1)	0.17 (0.07-0.40)	0.17 (0.07-0.41)	<0.001
	Sub-optimal SF >1000ng/mL (n=196)	**Optimal SF≤1000ng/mL (n=97)**			
Knew about a cure for thalassaemia n (%)	172 (87.8)	83 (85.6)	1.20 (0.59-2.45)	1.01 (0.47-2.15)	0.32
Accurate knowledge on HSCT n (%)	53 (27.0)	14 (14.4)	2.19 (1.14-4.20)	2.18 (1.12-4.21)	<0.05

HSCT: Haematopoietic stem cell transplantation, Hb: Haemoglobin, SF: Serum ferritin, CI: confidence interval

Table 5: ***Association between maternal knowledge on curative therapies and psychological health of their children***

Maternal knowledge	Emotional symptoms (n=55)	No emotional symptoms (n=249)	Unadjusted odds ratio (95%CI)	Adjusted odds ratio (95%CI)	p-value
Knew about a cure for thalassaemia n (%)	42 (76.4)	221 (88.8)	0.40 (0.19-0.85)	0.42 (0.19-0.95)	<0.05
Accurate knowledge on HSCT n (%)	01 (01.8)	67 (27.1)	0.04 (0.01-0.36)	0.05 (0.01-0.38)	<0.01
	Conduct symptoms (n=57)	**No conduct symptoms (n=247)**			
Knew about a cure for thalassaemia n (%)	46 (80.7)	217 (87.9)	0.57 (0.27-1.23)	0.76 (0.34-1.71)	0.51
Accurate knowledge on HSCT n (%)	02 (03.5)	67 (27.1)	0.09 (0.02-0.41)	0.10 (0.02-0.43)	<0.01
	Hyperactivity symptoms (n=29)	**No hyperactivity symptoms (n=275)**			
Knew about a cure for thalassaemia n (%)	24 (82.8)	239 (86.9)	0.72 (0.25-2.01)	1.01 (0.34-3.00)	0.97
Accurate knowledge on HSCT n (%)	0	69 (25.1)	-	-	<0.01*
	Abnormal peer relationships (n=45)	**Normal peer relationships (n=259)**			
Knew about a cure for thalassaemia n (%)	29 (64.4)	234 (90.3%)	0.19 (0.09-0.40)	0.35 (0.15-0.77)	<0.05
Accurate knowledge on HSCT n (%)	01 (02.2)	68 (26.3%)	0.06 (0.01-0.47)	0.09 (0.01-0.69)	<0.05
	Abnormal social behaviour (n=8)	**Normal social behaviour (n=296)**			
Knew about a cure for thalassaemia n (%)	07 (87.5)	256 (86.5)	1.09 (0.13-9.12)	0.81 (0.08-7.86)	0.85
Accurate knowledge on HSCT n (%)	03 (37.5)	66 (22.3)	2.09 (0.48-8.97)	2.10 (0.46-9.53)	0.33

* Chi-square test

Discussion

In this paper, we presented the findings of one of the largest studies assessing maternal knowledge on curative therapies among paediatric patients with TDBT. The study included 304 children, which comprised over 60% of the paediatric population with TDBT in Sri Lanka. Also, we evaluated the association between maternal knowledge on curative therapies on current medical treatment and psychological health among children with thalassaemia. We found that maternal knowledge on curative therapies in the study population was relatively low. Although 86% of parents knew that thalassaemia could be cured by HSCT, a very low proportion of them had the appropriate in-depth knowledge of the procedure. Only one-fifth knew that the HLA-matched sibling is the most suitable donor for HSCT, and a similar proportion accurately knew the cost of the procedure. Importantly only 1% recognised gene therapy as a developing cure. Less than half were aware of the fact that unrelated HLA-matched individual could be the donor, and less than 1% knew that cord blood could be used as a source of HSCs. These low figures were not expected in a country with a high literacy rate and easy and free access to health care like Sri Lanka. Specifically, this reflects the lack of enthusiasm and commitment among the medical teams providing the necessary knowledge to the patients. This is further reflected by the fact that only one-fourth of these children have undergone HLA-typing.

As expected, higher educational level in mother and father, as well as higher income, were associated with maternal knowledge on curative therapies of thalassaemia. Similar findings were reported by studies from the same region. For example, Manzoor I, *et al* reported poor parental knowledge of screening services for thalassaemia major among mothers who were housewives, had a lower education level and had lower family income[23]. One important finding of our study is that having an accurate knowledge on HSCT was associated with a lower prevalence of hepatomegaly and splenomegaly. This is important as hepatomegaly and splenomegaly indicate worsening of extramedullary haematopoiesis and sub-optimal blood transfusions[24]. Thus, knowledge on curative therapies seems to generate hopes for a cure in these patients, which has possibly motivated them to obtain blood transfusions on time. Our results correspond with the findings of a study on β-thalassaemia patients in Taiwan, which reported a positive association between knowledge about the disease and treatment adherence[25].

The most significant finding of our study is the report of a significantly lower prevalence of psychological symptoms among children of parents with accurate knowledge on curative therapies. This clearly shows that a better understanding of the disease and knowledge on the availability of a cure by the family is psychologically advantageous to children with thalassaemia, even if they do not have plans to undergo these procedures in the near future. This is especially important as patients with thalassaemia are reported to have a higher prevalence of psychological symptoms than the normal population[26]. As our study recruited over half of the paediatric thalassaemic population of Sri Lanka, the results are generalisable to the entire country. Similarly, the three study sites are situated in three discrete provinces and function as tertiary referral centres for the entire country, further improving the validity of the study. Also, β-thalassaemia is a rare disease globally; thus, a study involving over 300 participants of the disease is not easy to perform anywhere in the world[27]. Considering the scale of the study, our results would be useful to guide education, assessment, and management of patients with β-thalassaemia globally.

One important limitation of the study is that we only looked at maternal knowledge and did not evaluate the knowledge of patients themselves. Patient knowledge and attitude is an important factor in predicting the outcome and quality of life in chronic diseases, especially among older children[28]. Also, our study did not involve fathers. However, this may not have a major impact as in the cultural context of Sri Lanka, care for a sick child is mainly provided by mothers, and the female literacy rate in the country is over 90%, which is comparable to that of males. Based on the results of the study we recommend that all children with thalassaemia and their families are provided with current, accurate and up-to-date information on curative therapies which are available or in the development.

Conclusions

This study demonstrated that maternal knowledge on curative therapies among patients with β-thalassaemia is sub-optimal. It further demonstrated that having an accurate maternal knowledge is associated with improved medical care and a lower prevalence of psychological symptoms among patients.

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