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Original Research Article

A Cross Sectional Study for Growth and Quality of Life Assessment among Multitransfused Thalassemia Patients and Factors Affecting it in Kumaon Region of Uttarakhand, India

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Abstract

Background: Thalassemia is the most common genetic disorder worldwide and widely found in the tropical and subtropical regions of Mediterranean countries. These patients need frequent and lifelong transfusions that affects their growth and quality of life. This study evaluate growth and quality of life and factors affecting it in multitransfused Thalassemia patients.

Material and Methods: A cross sectional study was conducted on 60 Beta Thalassemic and 60 healthy matched controls of 2-16 years. WHO charts for growth and PedsQL^{TM} 4.0 Generic core scale was administered for quality-of-life assessment.

Results: This study showed 36.7% were moderate and 10% were severely undernourished while 28.3% were moderate and 15%were severely stunted among thalassaemic children. Maximum cases of stunting and undernutrition belonged to 5-10 years age with pre-transfusion hemoglobin <8gm/dl, serum ferritin 1500-3500ng/dl and frequent transfusions. Also, quality of life was poorly affected with mean score 46.27±3.02 in cases when compared to controls 87.50±1.52. Physical functioning scored the lowest followed by emotional, social and school. Quality of life was poorly affected by factors like low pre transfusion haemoglobin levels, frequent transfusions and poor compliance for chelation therapy. However, there was no association found between quality of life and serum ferritin levels in our study.

Conclusion: Findings in our study shows that regular blood transfusions with growth monitoring and proper chelation therapy is important and can improve both growth and quality of life in thalassemia patients.

Keywords: Beta thalassemia, Pre-transfusion hemoglobin, quality of life, Growth.

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Introduction

Thalassemia is an autosomal recessive disorder characterized by defect in synthesis of hemoglobin. [1] Most frequently, this disorder is found in the tropical and subtropical regions of Mediterranean countries, the Middle East, Central Asia, the Indian Subcontinent (South Asia) and Southeast Asia. [2] It has

been estimated that in India nearly 8000-10000 new thalassemia [homozygous] cases are born every year. [3]

In India, there is 3-4% average prevalence of Beta thalassemia carriers which corresponds to 35 to 45 million. Several ethnic groups have a much higher prevalence (4-17%) [4-6].

In Indian children the main problem is failure to maintain adequate hemoglobin levels and poor compliance to regular chelation therapy. This leads to transfusional hemosiderosis which have detrimental outcome in form of hyperpigmentation, hepatic fibrosis & cirrhosis, growth failure, delayed puberty and endocrinopathies namely diabetes mellitus, hypogonadism, hypoparathyroidism, hypothyroidism. [7] Growth retardation seen in thalassemia patients is a consequence of severe anemia and low somatomedin activity. Somatomedin synthesis is reduced due to hepatic hemosiderosis. [8]

For a chronic disease such as thalassaemia, where lifelong management is required, its management and complications are well known to have adverse effect on quality of life. [9,10] The 23-item PedsQL 4.0 Generic Core Scale by Dr. James Varni encompass Physical Functioning (8 items), Emotional Functioning (5 items),Social Functioning (5 items), and School Functioning (5 items), and were developed through focus groups, cognitive interviews, pretesting, and field-testing measurement development protocols. The PedsQL 4.0 Generic Core Scales are comprised of parallel child self-report and parent proxy-report formats. [11,12] This study is to compare growth and quality of life among Thalassemic children with their healthy age matched children.

Materials and Methods

A cross sectional study was conducted among 60 thalassemic patients and 60 healthy matched controls of age group 2-16 years in a tertiary care centre in Haldwani, Uttarakhand. The research proposal was approved by the Institutional Ethical Committee (I.E.C) of the university. The study period was January 2021 to September 2022.A detailed history, examination was done and WHO growth charts were used to interpret growth. A PedsQL^{TM}4.0 pediatric core scale was administered for assessing quality of life.

Inclusion Criteria

All transfusion dependent Thalassemia children upto 16 years of age for comparing growth pattern with their healthy matched controls, children between 2-16 years of age for assessing the quality of life with informed consent were included.

Exclusion Criteria

Children <2yr or >16yrs of age for assessing quality of life, children with cognitive impairment and severe psychological disorders, parents not willing to give written informed consent and children suffering from chronic /acute debilitating illness and its associated complications not related to thalassemia were not enrolled in the study.

Statistical Analysis

Statistical analysis was performed using SPSS software (SPSS Inc., Chicago, IL, USA) for the Windows program (16.0 version). The continuous variables were evaluated by mean (standard deviation) or range value when required. The dichotomous variables were presented in number/frequency and were analyzed using Chi-square or Fisher Extract test. A p-value of < 0.05 or 0.001 was regarded as significant.

Anthropometric Measurements

Weight- recorded with light clothing accurately on a lever or electronic type of weighing scale. The weighing scale

should be corrected for any zero error before measurement.

Height- measured in upright position. Heels are slightly separated and the weight is borne evenly on both feet. Back of head, shoulder blades, buttocks and heels all touching the vertical board/wall. The trunk should not lean backward or forward. The head is so positioned that the child looks directly forwards with Frankfort plane (the horizontal line joining the root of ear canal to lower margin of orbit) and the biauricular plane being horizontal. In this position head board pulled down to rest firmly on head with compressing hair. Now the measurement was read in Centimeters.

Body Mass Index=calculated as weight (kg) divided by height (m^2).

BMI = Weight (Kg)

Height (m^2)

Measurements were evaluated using WHO growth charts.

Interpretations

All weight for age, height for age and weight for height of median±2SD was normal, -3SD to -2SD was moderate undernutrition, stunting or wasting respectively and <-3SD was severe undernutrition, severe stunting and severe wasting.

Study Plan

Ethical Approval and informed consent were taken. The general biodata of the patient regarding their Name, age, sex, occupation and address, which presents in was collected. Selection of Patients was based on inclusion criteria. A detailed History with special reference on the onset and days of the presentation was taken. A complete General physical and systemic examination was done with anthropometric measurements. Socioeconomic status of the patients was evaluated using Modified Kuppuswamy Scale. All patients were subjected to complete hemogram, serum ferritin levels, hepatitis C and Hepatitis B serology. All patients were evaluated based on Questionnare used in our study PedsQL Generic 4.0 scale for assessment of quality of life in thalassemia patients. Secrecy and Confidentiality were maintained.

Results

The mean± SD age was 7.92± 3.34 years in cases and 8.32±3.40 years in control. Majority (45%) of cases were of age group 5-10 years ,28.3% belonged to < 5 years and 26.7% were > 10 years of age. There was male preponderance with 56.7% and about 40% cases belonged to Muslim community. Based on socio-economic status, majority (56.7%) of the participants belonged to lower middle socioeconomic status. There were 4 (6.7%) HCV positive patients found in present study. Majority of patients (88.3%) had pre transfusion haemoglobin levels of <8gm/dl and only 11.7% cases had levels >8gm/dl. The mean pre-transfusion hemoglobin levels were 6.96 gm/dl.

Only 20% cases had serum ferritin levels <1500ng/ml and rest 80% had levels >1500ng/ml. Mean serum ferritin levels were 2149±704.15. Only 53.3% cases had good compliance for iron chelation therapy and 46.7 % had poor compliance. Majority of patients (63.3%) required blood transfusions 2-3 times per month followed by 36.7% who required transfusions once per month. The mean age of starting transfusion was 7.05 months.

In our study we found there is significant growth retardation present in thalassemic children. 36.7% of patients were moderately undernourished (-3sd to -2sd) and 10% were severely undernourished (<-3sd). The mean±SD weight was 18.45± 5.13 Kgs in cases and 25.76±9.70 Kgs in control. Thalassemic patients also showed stunting 28.3% were moderate (-3sd to -2sd) while 15.0% were severely stunted

(<-3sd). The mean±SD height was 113.75±13.41 in cases and 126.13±20.09 cm in control. Wasting was also significant finding in the cases with 8.3% and 6.7% being moderate and severe wasting respectively. Body mass index of the patients was found to be normal in maximum (51.7%) cases but in around 40% cases low BMI was observed. But none of the control when compared with cases showed undernourishment, stunting, wasting or low BMI.

In our study we also found that quality of life is severely affected with mean score of 46.27±3.02 in cases and 87.50±1.52 in controls which was assessed by a questionnaire Pediatric Quality of Life Generic 4.0. All domains such as physical, social, emotional and school functioning were affected. The mean score for different domains were physical (33.12±6.49) followed by emotional (49.42±4.42), social (49.58±4.04) and school functioning (52.67±4.27).

There was significant correlation found between poor quality of life with pre-transfusion haemoglobin levels<8gm/dl (mean45.73±2.16), increased frequency of transfusions (mean48.86±3.06), poor compliance for iron chelation therapy (mean score50.19±2.19).

Table 1: Relationship between age of the patients and different anthropometric parameters

		Age Group			Total	Chi-square value	p-value
		< 5	**5-10.0**	**> 10**			
weight/age	at -3sd to -2 sd	17	23	14	54	2.695	0.260
	< -3sd	0	4	2	6		
height/age	at -3sd to -2 sd	15	23	13	51	0.317	0.854
	< -3sd	2	4	3	9		
weight/height	at -3sd to -2 sd	13	6	0	19	1.709	0.191
	< -3sd	4	0	0	4		
BMI(SD)	at -3sd to -2 sd	14	21	11	46	0.886	0.642
	< -3sd	3	6	5	14		
Total		17	27	16	60		

This table shows that maximum cases of stunting,wasting and undernutrition were found to be of age group 5-10 years. However, the results were not significant (p value>0.05).

Table 2: showing Mean for pediatric quality of life score and its different domains

	Cases		Control		t	p-value
	Mean	**SD**	**Mean**	**SD**		
Pediatric quality of life total score mean	**46.27**	**3.06**	**87.50**	**1.52**	**-93.346**	**0.001**
physical mean	33.12	6.49	84.77	2.29	-58.108	0.001
social mean	49.58	4.04	88.00	2.64	-61.650	0.001
school mean	52.67	4.27	90.08	0.65	-67.187	0.001
emotional mean	49.42	4.42	88.50	2.49	-59.653	0.001

Table 3: Correlation of Pediatric quality of life score with different parameters

	Age (yrs)	Weight (kg)	Height (cm)	BMI	Age of start transfusion (months)	Age of starting chelation (yrs)	Pretransfusion hemoglobin levels (gm/dl)	Serum ferritin levels
Correlation Coefficient	0.021	0.030	-0.039	-0.040	0.100	0.083	-0.475	0.111
p-value	0.874	0.823	0.766	0.764	0.448	0.527	0.001	0.398
N	60	60	60	60	60	60	60	60

Table shows that there was positive correlation of Pediatric quality of life score with pre transfusion hemoglobin level ((P<0.05).

Discussion

During our study we found that maximum cases of stunting, wasting and undernutrition belonged to age group of 5-10 years with pre-transfusion haemoglobin levels <8gm/dl and serum ferritin levels of 1500-3500ng/dl and had frequent blood transfusions (2 times per month). In our study most patients were inadequately transfused and poorly chelated with high serum ferritin levels which can be the cause of poor growth in these patients .However we did not find any significant co-relation between growth retardation and pre-transfusion haemoglobin levels or serum ferritin levels which is similar to the study of Gomber S et al. [13] Despite free transfusions and iron chelation therapy for Thalassemic children ,there are many challenges at every step in treating these patients. In these children, growth is significantly affected by multiple factors. The causes of short stature can be chronic anemia with ineffective erythropoiesis, micronutrient deficiency like zinc and folate, iron overload due to multiple transfusions, high serum ferritin levels, poor iron chelation therapy and other endocrine dysfunctions. [14,15]

There was significant correlation found between poor quality of life with pre-transfusion haemoglobin levels<8gm/dl, increased frequency of transfusions, poor compliance for iron chelation therapy in these patients which is like the findings in study by Mikael et al. [16] Jaihara et al found that there was a significant association between the total quality of life and compliance with blood transfusion and regular iron chelation therapy in both child and parent report. [17]

There was no association found between quality of life and serum ferritin levels in our study like the study by Lubis et al [18], Gomber S et al [13]. In contrast with our study, Hakeem et al found high serum ferritin levels significance with poor social quality of life. [19]

Conclusion

The primary goal of the present study was to study growth and assess quality of life in multitransfused thalassemia patients. In this study, 60 cases were enrolled with 60 age matched healthy children taken as controls. A cross-sectional study was performed. Most of the patients were between the age group of 5-10 years. Male preponderance was observed among patients (M:F ratio- 1.3:1). It was found that there was significant growth retardation, acute and chronic or acute on chronic, in Thalassemic children when compared to the control group. It was also found that most of the cases in our study had low pre transfusion haemoglobin levels with high serum ferritin levels and poor compliance for iron chelation therapy which can be the cause of undernutrition, stunting or wasting in these children. Thalassemia patients requiring regular

blood transfusion need better strategies for removing excess iron from their body. Thus, along with maintaining hemoglobin level, it is important to have effective iron chelation therapy to minimize retardation of growth in patient with transfusion-dependent thalassemia

Our study also concluded that all domains of life such as physical, social, school and emotional functioning are affected in these children. Physical functioning scored the lowest followed by emotional then social and school. Quality of life is significantly affected by low pre transfusion haemoglobin levels, iron overload and poor chelation therapy.

Limitations of Our Study

- We could not study the causes of growth failure or hormonal assays like GH (growth hormone) levels, IGF-I (Insulin-like growth factor) concentrations due to financial constraints.
- Imaging was also needed to be done to detect iron overload at different parts of the body but again high cost of these tests limit their usage.
- Another cause of anemia and growth retardation in Thalassemic patients is micronutrient deficiency (such as zinc, folate) but their levels also could not be assessed in our study.

Recommendations

- In our study, none of the patient had pre transfusion hemoglobin levels of >9gm/dl which is required for optimum growth and development therefore, we recommend that more hospitals or health care centers should provide free transfusions, blood tests and medications to Thalassemic children so that they do not require to travel far from their homes to maintain adequate hemoglobin levels. This often helps in relieving their financial burden and also improves quality of life to some extent.
- 4% of our study population was Hepatic C reactive, which is a chronic disease and can lead to heapatocellular carcinoma in future. This can be avoided by proper screening of the blood products before transfusion. Screening should be ensured for other infections also like Hepatitis B, HIV, etc in these patients.
- In this study, about 50% patients were undernourished, around 45% were stunted and 40% were wasted. Therefore, regular growth monitoring should be done for timely detection of growth retardation and its management.
- Different hormonal assays such as GH (growth hormone) levels, IGF-I concentration and imaging can be done to look for cause of growth retardation or delayed pubertal spurt.
- In our study, almost all Thalassemic patients had their quality of life affected in all domains when compared to their healthy matched controls. We recommend psychosocial support by counseling at day care centers or hospitals of both child and parents should be done to improve their quality of life.

Declaration of Interest

The authors report no conflicts of interest.

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None

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