Editorial

A study on growth profiles in children with thalassemia major between 2-10 years of age on regular transfusions and oral chelation therapy

Simhachalam M.[1], Sahoo M[2], Kuppili U.[3]

[1]Dr. Simhachalam Malluvalasa, Assistant Professor, [2]Dr. Manasranjan Sahoo, Associate Professor, [3]Dr. Uma maheswrararao Kuppili, Professor, all authors are affiliated with Department of Paediatrics, ASRAM Medical College, Eluru, Andhra Pradesh, India.

Corresponding Author: Dr. Simhachalam Malluvalasa, Assistant Professor, Department of Paediatrics, ASRAM Medical College, Eluru, Andhra Pradesh, India. Email: getmsc.doc@gmail.com

Abstract

Introduction: Thalassemia patients require regular blood transfusions to maintain haemoglobin level around 10gm/dl, which results in transfusional iron over load which is treated by well-established parenteral desferrioxamine or oral chelators. There are conflicting reports on effectiveness of oral chelators. Only few studies are available on the growth parameters of thalassemic children from this region. The present study was undertaken to assess the growth pattern and its relation with Mean Pre-transfusion Haemoglobin value and Serum ferritin concentration in study population. **Materials and Methods:** The present study was done at Thalassemia and Sickle CellSociety, Hyderabad. The study group includes Transfusion dependent thalassemia major children on oral Iron Chelation Therapy between 2-10 years of age. Specific inclusion and exclusion criteria were framed and subjects fulfilling the criteria were selected for the study. Anthropometry of the children was measured and necessary data from the medical records of the children was reviewed during the study period September 2012 to May 2013. **Results:** In Mean pre transfusion haemoglobin <8 g/dl group, all the children are below median weight for age and Height for age Z scores whereas in Mean pre transfusion haemoglobin ≥8g/dl, group, 12.3% of the children are above the median Weight for age Zscore and 6.2% of the children above the median Height for age Z score. Weight for age or Height for age Z scores has no correlation with age. With the increasing age, more thalassemic children had growth retardation, Height being affected more than Weight. **Conclusion:** Growth of thalassemic children during the first decade largely depends upon the maintenance of fairly normal haemoglobin between 9.5-10gm% with frequent blood transfusions and adequate chelation.

Key words: Chelation, Mean pre transfusion haemoglobin, Thalassemia, Z Scores

Introduction

The inherited hemoglobin disorders are the most common single gene defect in man. The frequency of the carrier state has been estimated to be 270/million with about 400,000 annual births a year of infants with serious hemo globinopathies world wide. The thalassemia syndromes are aheterogeneous group of Mendelian disorder characterized by lack or decreased synthesis of either α or β globin chains of haemoglobin. It results in ineffective erythropoiesis as well as lysis of mature red cells in spleen[1].

Epidemiology- The Thalassemias are the most common genetic disorder in a worldwide basis. 3% of world population carries genes of β thalassemia [2]. The β-thalassemias are wide spread through out the Mediterranean region, Africa, the Middle East, the Indian subcontinent and Burma, Southeast Asia including southern China, the Malay Peninsula, and Indonesia. Estimates of gene frequencies range from 3 to 10 percent in some areas [3]. There is evidence that the high frequency of β-thalassemia throughout the tropics reflects an advantage of heterozygotes against Plasmodium falciparum malaria[4].

Problem in India- In India over 20 million people have thalassemia gene. The prevalence of the gene varies between 3 to18% in north and 1 to 3% in south with certain communities like sindhis, kutchis, lohanas, bhanushalis, Punjabis, mahars, agris, gouds, etc. showing a high prevalence [4]. It has been estimated that over 6000-8000 children, who are homozygotes of

Manuscript received: 17th January 2018
Reviewed: 27th January 2018
Author Corrected: 4th February 2018
Accepted for Publication: 9th February 2018

ß-thalassemia are born in India every year and unfortunately most of these children die either undiagnosed because of inadequate facilities, poor management and/or financial constraints. There are only a few thalassemia units where these children are regularly given blood transfusion and monitored for various parameters. There are hardly any long-term studies of benefits of regular therapy and endocrine or cardiac complications from our country. Data is available only from few centres and as such no statistics are available regarding total number of thalassemics, their life expectancy, actual birth rates, causes of death. Majority of people still consider thalassemia as a curse rather than an inherited disorder [5].

Aims and Objectives

The present study was undertaken to

- To assess the growth pattern in Children with Thalassemia major on oral Iron chelation therapy.
- To compare the growth patterns across children with mean pretransfusion Haemoglobin <8 g/dl and ≥ 8g/dl.
- To assess ferritin concentration in transfusion dependent thalassemic children on oral chelation therapy, attending Thalassemia and sickle cell society, Hyderabad.

Materials and Methods

The present study was done at Thalassemia and Sickle cell Society, Hyderabad The study group includes Transfusion dependent thalassemia major children on oral Iron Chelation Therapy between 2-10 years of age. After taking proper consents the parents were interviewed through a structured questionnaire. Anthropometry of the children was measured and necessary data from the medical records of the children was reviewed during the study period September 2012 to May 2013.

Inclusion Criteria: The children between 2-10 years of age, who are diagnosed to have Thalassemia major based on HPLC (High performance liquid chromatography), receiving regular transfusions and on oral iron chelation therapy are included in the study.

Exclusion Criteria

1. Children <2yr or >10yrs of age.
2. The children who were not attending the Centre regularly for blood transfusion.
3. The children who were not started on oral chelation therapy or who are non-compliant with the oral chelation therapy.
4. The children with other co-morbid conditions like cardio myopathies, HBs Ag or HCV Positive or with other severe systemic illness.
5. Children who have undergone Splenectomy.
6. If the parents not willing to give consent.

Sample size calculation

The sample size was calculated using the following formula.

1. Estimate of the expected proportion (p)
2. Desired level of absolute precision (d)
3. Estimated design effect (DEFF)

The sample size formula is [6]:

$$n = \frac{1.96^2\, p(1-p)(DEFF)}{d^2}$$

Prevalence of Thalassemia in India = 3- 15% [7]
P = 0.05 (5%)

The estimated sample size =103. A total of 100 children were enrolled for the present study.

Method of collection of data: After explaining the parents about the study, informed consent was obtained. After taking prior consents from the parents in a prescribed format, they are interviewed using the proforma with a structured questionnaire including age, sex, details of their demographic data, age of diagnosis, frequency of transfusion, compliance to transfusion and chelation and their clinical data used.

Pretransfusion haemoglobin, during the last 6 blood transfusions was noted and mean calculated. Similarly, previous six Serum ferritin values were also reviewed from the records and mean calculated. Anthropometry and examination of the child were done. Socio economic status of the child has been classified according to the modi fied kuppuswamy scale [8].

Z score[9] : The deviation of the value for an individual from the median value of the reference population, divided by the standard Deviation for the reference population.

Z Score = (Observed value) - (Median reference value)/ Standard deviation of reference population

WHO Z scores were chosen for comparison because, they are more accurate for comparison than percentile charts. The group of total 100 children has been divided into two groups depending on the mean pre- transfusion haemoglobin <8 and >8 g/dl.

Student- t test and Mann whitney test has been used to find the significance of mean difference of Height and Weight Z scores in the two groups. Plotted on WHO Z score charts[10] and Calculated 'p' value to establish the significance of association.

Results

Age and sex distribution of the study- The study group includes total 100 transfusion dependent thalassemic children between 20-120 months of age. Among them, 70 are male children and 30 are female children.

Mean age of the study is 88.75 ± 22.18 months. Mean age of Male children is 85.94 ± 23.87 months. Majority of the children belongs to Hindu family i.e.60% (n=60) followed by Muslims 24% (n=24) and Christians 16% (n=16).

Consanguity- Majority of the children are born out of 2nd degree consanguity 51% (n=51), followed by Non consanguineous 39% (n=39) and 3rd degree Consanguity10% (n=10).

Mean Age of Diagnosis- Mean age of diagnosis was 6.74±3.69 months, youngest case being diagnosed at 2 months and oldest being 19 months. Mean age of diagnosis in Males was 6.48 ± 3.67 months and in females was 7.33 ± 3.74 months.

Distribution of Socioeconomic Status- Majority of the children belongs to Lower middle class 45% (n=45), followed by Upper middle 38% (n=38), Lower class10% (n=10) and Upper middle 7% (n=7) as per Modified Kuppuswamy classification [8].

Table -1: Percentage of children with Mean pre transfusionHb<8g/dl or ≥8g/dl

Mean Pre transfusion Hb%	Percentage
<8 g/dl	52% (n=52)
≥ 8g/dl	48%(n=48)

51 children in the current study had Mean pretransfusion Haemoglobin<8g/dl and 49 children had Mean pre-transfusion Haemoglobin≥8g/dl. Average pre-transfusion haemoglobin in the study group ranged from, 4.9 to 9.5g/dl with mean being 7.61± 1.41g/dl. Mean Pretransfusion Haemoglobin in males is 7.73±1.10 g/dl (Mean±SD) and in females is 7.71± 1.15g/dl (Mean±SD). There is no significant difference in Mean pre transfusion Haemoglobin between male and Female children.

Oral Iron Chelating agent used- Most of the children are on oral Deferiprone 63% (n=63), and 37% (n=37) of the children are on oral Deferasirox. Out of the 37 children on oral Deferasirox18.9% (n=7), children used Deferiprone previously and changed to Deferasirox because of complications (Arthropathy). Out of the 63 children on oral Deferiprone, 62% (n=29) children complaining of joint pains. No significant complications noted with Deferasirox during the study period. Probably because in all the children on Deferasirox the average duration of therapy is 3-8 months.

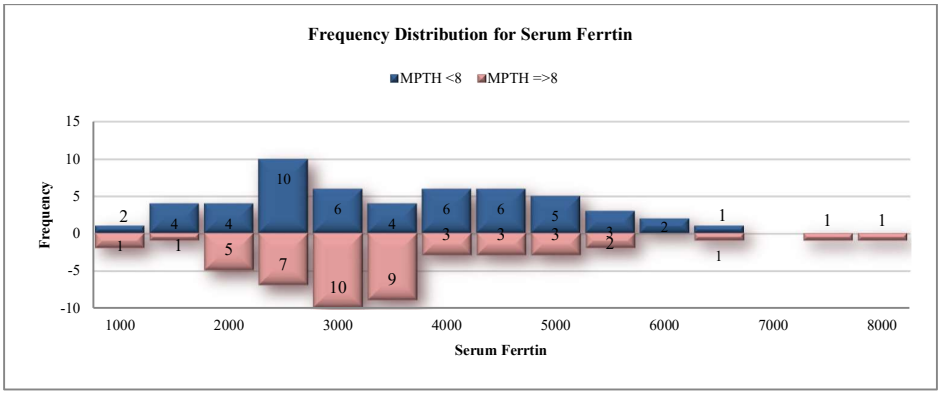

Figure -1: Comparison of Serum Ferritin concentrations across children with Mean pre transfusion Hb< 8g/dl and ≥8g/dl

In children with Mean pre transfusion Hb<8g/dl, the average Serum ferritin Concentration is 3501.36 ± 1390.76 ng/ml. (Mean ± SD) with Standard Error of 192.86 ng/ml. In children with Mean pre transfusion Hb ≥8g/dl, the average Serum ferrit in concentration is 3455.87 ± 1466.52ng/ml. (Mean ± SD) with Standard Error of 211.67 ng/ml.'P' value calculated using student t-test is 0.874**,** which is statistically not Significant, which means there is no significant difference in serum ferritin values between the two groups. (with 95% Confidence Interval).

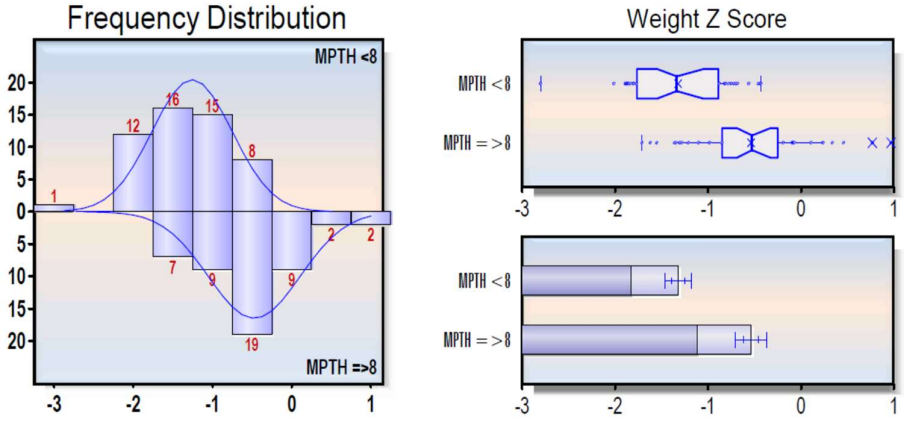

Figure 2: Comparison of Weight for age Z scores between children with Mean pre transfusion Hb< 8g/dl and ≥ 8g/dl

Table-2: Comparison of Weight for age Z scores between children with Mean pre transfusion Hb< 8g/dl and ≥ 8g/dl.

Weight for age Z score	MPTH <8 g/dl (n=52)	MPTH ≥ 8g/dl (n=48)
> 0	0 (0%)	6(12.5%)
0 to -1	15(28.8%)	33(68.7%)
-1 to -2	35(67.3%)	9(18.7%)
-2 to -3	2(3.8%)	0
< -3	0	0

The results are compared using Student t test and Mann whitney test. Mean, standard deviation and standard error of deviation are calculated. In children with Mean pre transfusion Hb<8g/dl, mean weight for age Z score Is-1.321±0.506 (Mean±SD), with Standard Error of 0.070. In children with Mean pre transfusion Hb ≥8g/dl, mean weight for age Z score Is-0.537±0.579 (Mean±SD), with Standard Error of 0.084.'P' value calculated using student t-test is **0.000,** which is statistically Significant that means there is significant difference WAZ scores between the two groups. WAZ scores of Male and Female children with Mean pre transfusion Hb<8g/dl and ≥ 8g/dl are compared.

Table-3: Comparison of Weight for age Z scores between male and female children with Mean pre transfusion Hb< 8g/dl and ≥ 8g/dl.

Observation	Males MPTH <8g/dl n=16(53.3%)	Males MPTH ≥8g/dl n=14(47.7%)	Females MPTH <8g/dl n=34(48.6%)	Females MPTH ≥8g/dl n=36(51.4%)
WAZ score Mean ± SD	-1.32± 0.52	-0.54±0.60	-1.32± 0.46	-0.42±0.45

Between male and Female children with Mean pre transfusion Hb<8g/dl'P' value for WAZ scores calculated using student t-test is **0.855,** which is statistically not Significant that means there is no correlation of sex with WAZ scores .Between male and Female children with Mean pre transfusion Hb≥8g/ dl'P' value for WAZ scores calculated using student t-test is **0.523,** which is statistically not Significant that means there is no correlation of sex with WAZ scores .

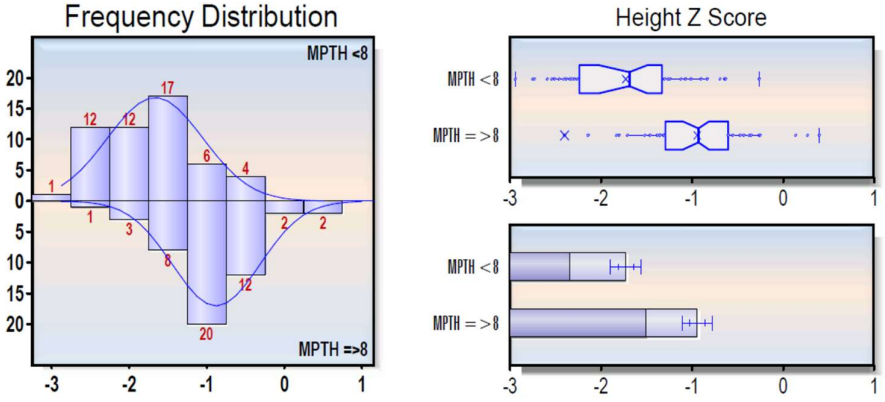

Figure- 3: Comparisonof Height for age Z scores between children with Mean pre transfusion Hb<8g/dl and ≥8g/dl

Table-4: Comparison of Height for age Z scores between children with Mean pre transfusion Hb<8g/dl and ≥8g/dl.

Height for age Z score	MPTH <8 g/dl (n=52)	MPTH ≥ 8g/dl (n=48)
> 0	0(0%)	3(6.22%)
0 to -1	7(13.4%)	22(45.8%)
-1 to -2	25(48.2%)	21(43.7%)
-2 to -3	20(38.4%)	2(4.1%)
< -3	0	0

In children with Mean pre transfusion Hb<8g/dl, mean Height for age Z score is -1.728 ± 0.616 (Mean±SD), with Standard Error of 0.085. In children with Mean pre transfusion Hb ≥8 mg/dl, mean Heightfor age Z score is-0.943 ± 0.561 (Mean ± SD), with Standard Error of 0.081.'P' value calculated using student t-test is **0.000,** which is statistically Significant that means there is significant difference in HAZ scores between the two groups. HAZ scores of Male and Female children with Mean pre transfusion Hb<8g/dl and ≥ 8g/dl are compared.

Table-5 Comparison of Height for ahe Z scores between male and female children with Mean pre transfusion Hb< 8g/dl and ≥ 8g/dl

Observation	Males MPTH <8g/dl n=16(53.3%)	Males MPTH ≥8g/dl n=14(47.7%)	Females MPTH <8g/dl n=34(48.6%)	Females MPTH ≥8g/dl n=36(51.4%)
HAZ score Mean ± SD	-1.69± 0.64	-0.89±0.58	-1.79± 0.55	-1.05±0.48

Between male and Female children with Mean pre transfusion Hb<8g/dl'P' value for HAZ scores calculated using student t-test is **0.584,** which is statistically not Significant that means there is no correlation of sex with HAZ scores. Between male and Female children with Mean pre transfusion Hb≥8g/dl.'P' value for WAZ scores calculated using student t-test is **0.379,** which is statistically not Significant that means there is no correlation of sex with WAZ scores.

In children with Hb<8 g/dl, 50% (n=26) of the children had Hyper pigmentation and in children with mean pre transfusion Hb ≥8g/dl 58.3% (n=28) of the children had hyper pigmentation. In children with Hb<8 g/dl,78.8% (n=41) of the children had facial changes and in children with mean pre transfusion Hb ≥8g/dl, 85.4% (n=41) of the children had facial changes. Both the groups compared using student t test and 'p' value calculated is 0.397 for facial changes and 0.408, both are statistically not significant that means, there is no correlation of MPTH with the incidence of Hyper pigmentation or facial changes.

The study population has been divided into three groups based on age.

Table-6: Division of study population into three age groups

Age group	n = (no.of children)
25-84 months	34(34%)
84-108 months	44(44%)
108-120 months	22(22%)

Mean Pre transfusion Hb, Mean Serum Ferritinare compared and Mean, Standard deviation calculated.

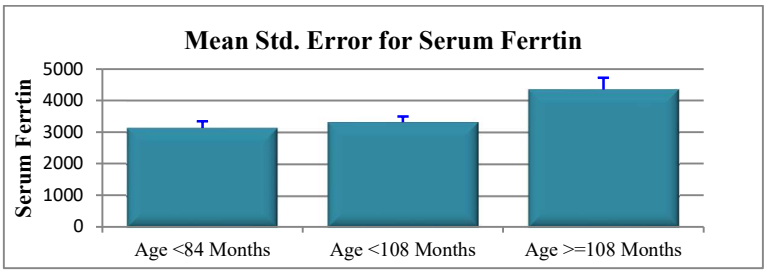

Figure-4: **Mean Serum ferritin values between the three age groups**

Mean Serum ferritin value for the Age 20-84 months (Mean±SD) is3132.18 ± 1219.76 ng/ml (n=34).Mean Serum ferritin value for the Age 84-108 months (Mean±SD) is 3315.45±1210.10 (n=44). Mean Serum ferritin value for the Age 108-120 months (Mean±SD) is 4344.50±1772.34 (n=22). The three age groups compared using ANOVA(p=0.004) and Kruskal Wallis H test (p=0.020), concludes that there is significant increase in Serum Ferritin values with age.

Table-7: Mean Pre transfusion Haemoglobin in g/dl between the three age groups.

Observation	Age 20-84 months (Mean±SD)	Age 84-108 months (Mean±SD)	Age 84-120 months (Mean±SD)
MPTH in g/dl	7.48±1.01	7.75±1.18	8.00±1.11

The mean pre-transfusion Haemoglobin in all the three age groups waswell below the recommended level of 9.5-10 gm% for adequate growth of Thalassemic children. However it was slightly higher in the elder children but it was not significant statistically (p=0.225) means, MPTH value has no correlation with the age.

Discussion

The present study is a cross sectional study of the growth pattern and serumFerritin levels in transfusion dependent thalassemic children between 2-10yrs of age on oral chelation therapy. Children with MPTH<8g/dl and ≥8 g/dl are compared for growth parameters.

In the study conducted by Harish K Pemde, Jagdish Chandra, Divya Gupta etal[11]a cross-sectional analysis of the records of the patients registered at and being followed up by the Thalassemia Day Care Centre (TDCC) at Kalawati Saran Children's Hospital, Delhi, Z-scores for weight, height, and body mass index (BMI) were calculated using World Health Organization reference data and compared.

In the study conducted by Tienboon P, Sanguansermsri Tetal [12], 115 Non Splenectomised children (6 months-6 years, 54 males, 61 girls) with beta thalassemia major who has not previously received chelation therapy compared using WAZ (Weight for age Z scores) and HAZ (Height for age Z scores). Descriptive statistics variables studied in the present study were comparable to other studies. [11,12,13]

Mean age of diagnosis: The finding in the present study on age of diagnosis correlates with study by Prita et al[14] who observed 75.8% of cases were diagnosed below 2 years. Thalassemia major (Homozygous) manifests very early in childhood with pallor being obvious with in the first year of life. In the present, study all the children diagnosed below 19 months of age.

History of consanguinity was present in 61% in the present study and this correlates well with Reddy et al[15] study which showed that 70% of the patients were the product of second degree consanguineous marriage.

Mean pre transfusion haemoglobin level- Mean Pre transfusion haemoglobin level in the present study was 7.61±1.41 g/dl This is well below the recommended level of 9.5-10 gm% for adequate growth of thalassemic children.

49% (n=49) children in the study had mean Pretransfusion haemoglobin of less than 8g/dl compared to 44.2 percent of children in study conducted by Anice George, et al[16], indicating inadequate transfusion. MPTH values were compared between male and female children in the study group using student t test. No significant association could be established (p=0.998). Most of the children in our study belong to Lower middle and upper lower Socio economic classes

Iron Chelating agent- In the current study most of the children are on oral Deferiprone n=63(63%), and n=37 (37%) of the children are on oral Deferasirox compared to Deferiprone (72%), and Deferasirox (25%) in the study by Harish K Pemde, etal[11].

Table -8 : Comparison of Serum Ferritin levels with similar studies

Studies	Serum ferritin ng/ml (Mean±SD)
Harish K Pemdeetal[11]	3112 ± N/A
V.P Choudhry[5]	3785 ± 2876
Sunil Gomber et al[17]	3422.65 ±1581.01
Present study	MPTH <83501.36±1390.7
	MPTH ≥83455.87±1466.5

In the present study mean Serum ferritin levels in both the groups were approximately three times (>3400ng/mL) the desired value despite the patients being on deferiprone n=63 (63%) or deferasiroxn=37(37%).

The mean Serum ferritin correlates with the study of Sunil Gomber, et al[17],V.P Choudhry [5] who observed the similar Serum Ferritin values despite adequate chelation with Deferiprone.Harish K Pemdeetal [11] in their study conclude that the mean serum ferritin levels were approximately 3112 ng/mL the desired value despite the patients being on deferiprone (72%) or deferasirox (28%).

These findings cast doubt over the ability of the oral chelation therapy to reduce the iron burden in thalassemic children, at least in short period. In her study Olivieri NF, etal [18] Concluded, Deferiprone does not adequately control body iron burden in patients with thalassemia and may worsen hepatic fibrosis.

Serum ferritin values also compared with in three age groups in the present Study. Among the three different age groups in the current study the serum Ferritin values increased significantly. The Linear regression coefficient computed between the age groups showed between <84 months and 84-108 months the rise in mean serum ferritin value is 182.43, where as between 84-108 months and >=108 months group, the rise in mean serum ferritin value is 377.86ng/ml .

In the study by Harish K Pemdeetal [11], Linear regression coefficient showed that for every 1-year increase in age, the mean ferritin value increased by 186.21 pg/mL (95% CI: 143.31–228.27) which is comparable.

Weight for age Z scores- All the children with Mean pre transfusion Hb<8g/dl, are below the median Z score (n=52) 100%, i.e. under nourished.3.8% (n=2) of them falls into moderate malnutrition. 67.3% (n=35) of the children are between -1 to -2 SD. 28.8% (n=15) of the children are between 0 to -1 SD. None of them are severely wasted. In children with Mean pre transfusion Hb≥8 mg/dl, (n=49),12.5% (n=6) of the children are above the median. 18.7% (n=9) of the children are between -1 to -2 SD.

68.7% (n=33) of the children are between 0 to -1 SD, compared to 28.8% (n=15) in children with Mean pre transfusion Hb<8g/dl. 'P' value computed for correlation of WAZ scores using student t-test is 0.000, which is statistically significant. That means there is significant difference in weight for age between the two groups.

WAZ scores are also compared between male and females in both the groups using student t test. In children with Mean pre transfusion Hb<8 mg/dl, males and females compared using student t test, and the 'p'value is, 0.855 which is not significant. In children with Mean pre transfusion Hb≥8 mg/dl, males and females compared using student t test and the 'p'value is 0.523 which is not significant.

In the study by Teinboonetal [12] concludes that most children had abnormal weight-for-age (WAZ) and height-for-age (HAZ) Z scores, however female children had lower WAZ and HAZ compared to males. In the study by Harish K Pemdeetal[11] 13% were thin, and 10.82% were very thin (BMI z-score <-3), in patients with pre transfusion Hb levels maintained at desired levels physical growth was correlated with status of iron overload.

Height for age Z scores- All the children with Mean pre transfusion Hb<8g/dl, are below the median HAZ score (n=52)100% i.e low height for age.39.4% (n=20) of them falls between -2 to -3SD HAZ scores i.e. moderately stunted. 48% (n=25) of the children are between -1to -2 HAZ score.13.4 % (n=7) of the children are between 0 to - 1 SD HAZ score. None of them are severely stunted.

In children with Mean pre transfusion Hb≥8 mg/dl (n=48), 6.25% (n=3) of the children are above the median.4.1% (n=2) of the children are below -2 SD. 43.7% are between -1 to -2 SD.45.8% (n=22)) of the children arebetween 0 to -1 SD, compared to 13.4% in children with Mean pre transfusion Hb<8g/dl.'P' value computed for correlation of WAZ scores using student t-test is 0.000, which is statistically significant.

In the study by Tein boonetal [12], Most children had abnormal weight-for-age (WAZ) and height-for-age (HAZ) Z scores, however female children had lower WAZ ($p < 0.0001$) and HAZ ($p < 0.02$) compared tomales. In the study byHarish K Pemdeetal [11], One-third (33.11%) of the patients had short stature. In the present study 42.5% (n=22) of the children are short statured. Height z-scores had significant correlation with mean ferritin levels, whereas correlation with mean pre transfusion Hb was not significant statistically.

Conclusions

Majority of thalassemic children were product of consanguineous marriage. 51% children had mean Pretransfusion hemoglobin of less than 8gm%; mean being 7.61 g/dl, indicating inadequate blood transfusion. Oral chelation was not found to be effective in reducing the iron over load. Joint pains were observed in significant number of children when on Deferiprone. Number of children with growth retardation increased with increasing age and decreasing hemoglobin percentage, high ferritin levels and sub-optimal iron chelation therapy. Although, for most of the children Z scores for both height and weight for age ranged between -1 SD and -2 SD, with advancing age regression in these scores was obvious (fall in values was more prominent in height compared to weight). Overall, Z scores for height for age and weight for age were low. Genetic potential (Mid parenteral height) doesn't seems to have relation with the growth deviation. In developing countries, like India poor socio-economic background compounds the problem.

Growth of thalassemic children during the first decade largely depends upon the maintenance of fairly normal haemoglobin. Every attempt should be made to maintain the haemoglobin levels at 9.5-10gm% with frequent blood transfusions. Parents should be counselled about the importance of maintaining the adequate Haemoglobinl evels. Determination of serum ferritin and routine growth monitoring at regular intervals is necessary with increasing age, to detect any disturbance in growth and to establish appropriate management protocols.

What this study adds to existing knowledge- Although, for most of the children Z scores for both height and weight for age ranged between -1 SD and -2 SD, with advancing age regression in these scores was obvious (fall in values was more prominent in height compared to weight). Overall, Z scores for height for age and weight for age were low.Genetic potential (Mid parenteral height) doesn't seem to have relation wit the growth deviation.

Funding: Nil, **Conflict of interest:** None initiated,
Perission from IRB: Yes
Institutional Ethical committee approval: Yes

References

1.Kumar V. Disease of red cells and bleeding disorders. In: Robbins text book of pathology basis of disease, 5th edn. Cotran RS, Kumar V, and Robbins SL. India: WB Saunders, 1994, 583-627.

2. Quirolo Keith and Elliot Vichinsky. Thalassemia syndromes. In: Nelson Text book of Pediatrics, 19th edn. Behrman RE, Kliegman RM and Jenson HB (eds). India. Elsevier, 2012, 1674-78.

3. Weatherall DJ. The thalassemias. In: Stamatoyannopoulos G, Nienhuis AW, Majerus PH, Varmus H, eds. The molecular basis of blood diseases. 2nd ed. Philadelphia: W. B. Saunders, 1994: 157-205.

4. Weatherall DJ. Common genetic disorders of the red cell and the "malaria hypothesis" Annals of Tropical Medicine Parasitology 1987; 81:539-548.

5. Choudhry V.P, R. Kashyap,S.K. Acharya, N. Tandon, A. Saxena. Challenges in the Management of Thalassaemia, Mediquest Medical Information series - 1997: Vol. 15 : No.3: 1-9.

6.Gorstein J, Sullivan KM, Parvanta I, Begin F. Indicators and methods for cross-sectional surveys of vitamin and mineral status of populations. Micronutrient Initiative (Ottawa) and Centers for Disease Control and Prevention (Atlanta), May 2007, pg 29).

7. Thacker N. Prevention of thalassemia in India.Indian Pediatr. 2007 Sep;44(9):647-8.

8. Sharma R. Kuppuswamy's socioeconomic status scale--revision for 2011 and formula for real-time updating. Indian J Pediatr. 2012 Jul;79(7):961-2. doi: 10.1007/s12098-011-0679-3. Epub 2012 Jan 10.

9. WHO anthro software (www.who.int/childgrowth/ software.

10. http://www.who.int/childgrowth/standards

11. Pemde, Harish, Chandra Jagdish, Gupta Divya, Singh Varinder, Sharma, Rajni, Dutta, Ak. Physical growth in children with transfusion-dependent thalassemia. Pediatric Health, Medicine and Therapeutics. 2011. 2-13. 10.2147/PHMT.S15305.

12. Tienboon P, Sanguansermsri T, Fuchs GJ. Malnutrition and growth abnormalities in children with beta thalassemia major. Southeast Asian J Trop Med Public Health. 1996 Jun;27(2):356-61.

13. Singhal B, Shama N and Mathur R. Iron Overload and Growth of Thalassemic Patients in Marwar Region. Int J Pharm Sci Res, 2012; Vol. 3(7): 2043-2049.

14. Trehan P, Madan N, Ghai OP, Sood SK. Beta-thalassaemia syndromes as seen in Northern India. Indian Pediatr. 1980 Mar;17(3):219-26.

15. Reddy YR et al. Brief communication, thalassemia in Andhra Pradesh- a clinic haematological study. Indian paediatrics 1975; 12:195-199.

16. George A, Bhaduri A, Sen S, Choudhry VP. Physical growth parameters in thalassemic children. Indian J Pediatr. 1997 Nov-Dec; 64(6):861-71.

17. Sunil Gomber, Rohit Saxena, Nishi Madan. Comparative efficacy of Desferrioxamine, Deferiprone and in combination on Iron Chelation in Thalassemic Children. Indian paediatrics2004;41:21-26.

18. Olivieri NF, et al. Long-Term Safety and Effectiveness of Iron Chelation Therapy with Deferiprone for Thalassemia Major. New England journal of Medicine.1998; 339:417-423.

……..

How to cite this article?

Simhachalam M, Sahoo M, Kuppili U. A study on growth profiles in children with thalassemia major between 2-10 years of age on regular transfusions and oral chelation therapy. Int J Pediatr Res. 2018;5(2):78-86. doi:10.17511/ijpr.2018.i02.07.

……..