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GROWTH PROFILE AMONG CHILDREN WITH THALASSEMIA MAJOR ON REGULAR TRANSFUSIONS AND ORAL CHELATION THERAPY

Pediatrics

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ABSTRACT

Background: The inherited haemoglobin 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. The Thalassemia's are the most common genetic disorder in a worldwide basis. 3% of world population carries genes of β thalassemia[3].In India over 20 million people have thalassemia gene.It has been estimated that over 6000-8000 children, who are homozygotes of ß-thalassemia are born in India every year and unfortunately most of these children die either undiagnosed. **Objectives:** 1.To assess the growth pattern in Children with Thalassemia major on oral Iron chelation therapy 2.To compare the growth patterns across children with mean pre-transfusion Haemoglobin <8 g/dl and ≥ 8g/dl.**Materials and Methods:** The study was done in Transfusion dependent thalassemia major children on oral Iron Chelation Therapy between 2-10 yrs of age who are attending ASRAM Medical College, Eluru for regular transfusions. A total of 100 children was studied based on sample size calculated taking prevalence of 10% with 95% CL and absolute precision of 6%. **Results:** Out of 100 children, 70 were male and 30 were female. Mean age of the study population is 88.75 ± 22.18 months. Majority of the children are born out of 2nddegree consanguity 51% (n=51), followed by Non-consanguineous 39 % (n=39) and 3rddegree Consanguity 10%. Most of the children are on oral Deferiprone 63%(n=63),and 37%(n=37)of the children are on oral Deferasirox. In children with Mean pre transfusion Hb<8g/dl, the average Serum ferritin Concentration is 3501.36 ± 1390.76 ng/ml. In children with Mean pre transfusion Hb ≥8g/dl, the average Serum ferritin concentration is 3455.87 ± 1466.52ng/ml**.Conclusion:** Thalassemia syndromes are important cause of morbidity and mortality in children. Majority of thalassemic children were born to consanguineous marriage. Most of the children had mean Pre transfusion hemoglobin of less than 8gm% indicating inadequate blood transfusion. Oral chelation was not found to be effective in reducing the iron over load. Although the patients were on regular blood transfusions, they were maintaining low hemoglobin levels which is evident from positive association with growth parameters.

KEYWORDS:

INTRODUCTION:

The inherited haemoglobin 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 haemoglobinopathies worldwide. The prevalence of haemoglobinopathies is on the rise worldwide. This is of special importance in developing countries, where it increases the burden of health care delivery systems[1]. The thalassemia syndromes are a heterogeneous 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[2].The Thalassemia's are the most common genetic disorder in a worldwide basis. 3% of world population carries genes of β thalassemia[3].In India over 20 million people have thalassemia gene.It has been estimated that over 6000-8000 children, who are homozygotes of 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[4]. Blood transfusion, though a well-established form of therapy, is not available to the majority of thalassemics because of its limited availability.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. Majority of people still consider thalassemia as a curse rather than an inherited disorder[5].The present study was conducted with aim to assess the growth pattern in Children with Thalassemia major on oral Iron chelation therapy and to compare the growth patterns across children with mean pretransfusion Haemoglobin <8 g/dl and ≥ 8g/dl.

MATERIALS AND METHODS:

The study was done in Transfusion dependent thalassemia major children on oral Iron Chelation Therapy between 2-10 yrs of age who are attending ASRAM Medical College, Eluru, Andhra Pradesh for regular transfusions.A total of 100 children was studied based on sample size calculated taking prevalence of 10% with 95% CL and absolute precision of 6%.

Inclusion Criteria: The children between 2-10 yrs 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.

Exclusion criteria: 1.The children who were not attending the centre regularly for blood transfusion. 2.The children who were not started on oral chelation therapy or who are non-compliant with the oral chelation therapy. 3.Children who have undergone Splenectomy.

Parents were explained about the study in the local language in an understandable way. After taking consent from parents, they are interviewed using the proforma with a semi-structured questionnaire including socio-demographic profile, age of diagnosis, frequency of transfusion, compliance to transfusion and chelation and their clinical data used.Pre transfusion haemoglobin done by Sahli's method,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.Electronic digital weighing machine and Stadiometerwas being used to measure weight and height respectively.Data was entered and analyzed usingEpi info and Z-test was used to find out the significant difference between two groups.

RESULTS:

Out of 100 children, 70 were male and 30 were female. Mean age of the study population is 88.75 ± 22.18 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). Majority of the children are born out of 2nddegree consanguity 51% (n=51), followed by Non consanguinous 39 % (n=39) and 3rddegree Consanguity10% (Fig-1).51

children in the current study had Mean pre transfusion 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 to9.5g/dl with mean being 7.61± 1.41g/dl.Mean Pre transfusion Haemoglobin in males is 7.73±1.10 g/dl and in females is 7.71± 1.15g/dl. There is no significant difference in Mean pre transfusion Haemoglobin between male and Female children (p-value = 0.998). 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 Deferasirox, 18.9%(n=7),children used Deferiprone previously and changed to Deferasirox because of complications.In children with Mean pre transfusion Hb<8g/dl, the average Serum ferritin Concentration is 3501.36 ± 1390.76 ng/ml. In children with Mean pre transfusion Hb ≥8g/dl, the average Serum ferritin concentration is 3455.87 ± 1466.52ng/ml.There is no significant difference (p-value=0.874) in serum ferritin values between the two groups.In children with Mean pre transfusion Hb<8g/dl, mean weight for age Z score (Table-1) is 1.321±0.506 and In children with Mean pre transfusion Hb ≥8g/dl, mean weight for age Z score Is-0.537±0.579. There is significant difference (p-value <0.05) WAZ scores between the two groups.In children with Mean pre transfusion Hb<8g/dl,mean Height for age Z score(Table-2) is -1.728 ± 0.616 and in children with Mean pre transfusion Hb ≥8 mg/dl,mean Heightfor age Z score is-0.943 ± 0.561. There is significant difference (p-value = 0.000) in HAZ scores between the two groups.

DISCUSSION:

The present study was a Cross sectional study to assess the growth pattern and serum Ferritin 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. The age group of children in the present study were between 25-120 months. Mean age of male children was 85.94 + 23.87 months and female children was 85.94 + 23.87 months. History of consanguinity was present in 61% in the present study. Among that majority 51% were children of second degree consanguineous marriages. This correlates with Reddy *et al*[6] study which showed that 70% of the patients were children of second degree consanguineous marriage. Hence, consanguineous marriages have to be discouraged in affected families, to prevent the birth of a thalassemia child.Screening for carrier state should be done before marriage in people with family history. 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% of children in study conducted by Anice George *et al*[7], indicating inadequate transfusion. 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 (63%) or Deferasirox (37%). The mean Serum ferritin correlates with the study of Sunil Gomber*etal*[8], V.P Choudhry*et al*[9] and who observed the similar Serum Ferritin values despite adequate chelation with Deferiprone. 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,whereas between 84-108 months and >=108 months group, the rise in mean serum ferritin value is 377.86ng/ml. Study conducted by Harish K Pemde *etal*[10], showed that for every 1-year increase in age, the mean ferritin value increased by 186.21 pg/mL which was similar to the present study. 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 Z-test is 0.000, which is statistically significant. That means there is significant difference in weight for age between the two groups. 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. 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 are between 0 to -1 SD,compared to 13.4% in children with Mean pre transfusion Hb<8g/dl. This was similar to study conducted by Teinboon etal[11]which showed most children had abnormal weight-for-age (WAZ) and height-for-age (HAZ) Z scores.

CONCLUSION:

Thalassemia syndromes are important cause of morbidity and mortality in children. Majority of thalassemic children were product of consanguineous marriage. 51% children had mean Pre transfusion 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. Although the patients were on regular blood transfusions, they were maintaining low hemoglobin levels which is evident from positive association with growth parameters. 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.

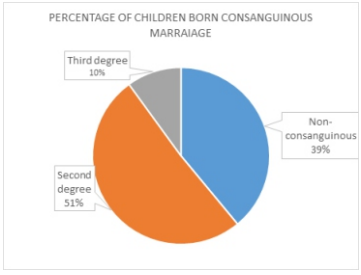
Table -1

S.No	Weight for age Z score	MPTH < 8g/dl (n=52)	MPTH > 8g/dl (n=48)
1.	>0	0(0%)	6(12.5%)
2.	0 to -1	15 (28.8%)	33 (68.7%)
3.	-1 to -2	35 (67.3%)	9 (18.7%)
4.	-2 to -3	2 (3.8%)	0

Table - 2

S.No	Height for age Z score	MPTH < 8g/dl (n=52)	MPTH > 8g/dl (n=48)
1.	>0	0(0%)	3(6.22%)
2.	0 to -1	7 (13.4%)	22 (45.8%)
3.	-1 to -2	25 (48.2%)	21 (43.7%)
4.	-2 to -3	20 (38.4%)	2 (4.1%)

Figure - 1



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