ISSN: 0975-3583,0976-2833 VOL13, ISSUE 04, 2022

A CROSS SECTIONAL STUDY TO ASSESS GROWTH AND DEVELOPMENT IN CHILDREN WITH THALASSEMIA AT TERTIARY CARE HOSPITAL

Dr. Srilatha Sivuni[1], Dr. Prathyusha Chiitti Boina Venkata[2], Dr. Sankar Narayana C[3], Dr. Lakshmi Prasanna Chintha[4*]

[1]Assistant Professor, Department of Pediatrics, Govt Medical College, Ananthapur.
[2]Assistant Professor, Department of Pediatrics, Govt Medical College, Ananthapur.
[2]Assistant Professor, Department of Pediatrics, Govt Medical College, Ananthapur
[4*]Assistant Professor, Department of Pediatrics, Siddartha Medical College, Vijayawada.

Corresponding Author: Dr. Lakshmi Prasanna Chintha
Assistant Professor, Department of Pediatrics, Siddartha Medical College, Vijayawada.
E mail:laksha82@gmail.com

Abstract

Introduction: The inherited hemoglobin disorders are the most common single-gene defect in man. The frequency of the carrier state is estimated to be 270 million, with about 400,000 annual births a year of infants with serious hemoglobinopathies. The present study was undertaken to assess the growth and development according to pretransfusion HB levels, to determine the growth and development according to serum ferritin levels.

Materials and Methods: The present study was a hospital-based on a prospective observational study conducted in tertiary care hospital Kurnool. The total number of cases are 50. The children diagnosed to have Thalassemia major based on hemoglobin electrophoresis, came for blood transfusion, and who were advised to take Deferiprone are included in the study. The children had a severe systemic illness were excluded. The study was approved by the ethical comity of Kurnool Medical College, Kurnool. Chi-square and Fisher exact has been used to find the association of age and mean pre-transfusion HB% and mean ferritin levels with weight & height for age as per IAP standard.

Results: Nearly 60% of cases (31) were boys. Out of that, 3 cases in <2 years, 7 cases between 2-5 years, 16 cases in the age group of 5–10 years, and 5 cases in the age group of 10-15 years. 19 cases out of 50 were girls. In the study on 50 thalassemia children, 62% were boys, and 38% were Girls. The mean age of diagnosis in Thalassemia Major was approximately 8.6 months. The minimum age of diagnosis was 3.6 months, and the maximum age of diagnosis was 2.5 years. The pre-transfusion hemoglobin of 36 cases was between 6 – 9 gm/dl in 72% of cases. 16% cases had levels less than 6 gm/dl, and only 12 % had pre-transfusion Hb levels above 9 gm/dl.

Conclusion: Thalassemia syndromes are a significant cause of morbidity and mortality in children. Most of the children had mean pretransfusion hemoglobin of less than 8 gm%, mean being 7.5 gm%, indicating inadequate blood transfusion. Growth retardation was a significant problem in thalassaemic children. The number of children with growth

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 04, 2022

retardation increased with increasing age and decreasing hemoglobin percentage, indicating chronic hypoxia may be responsible for the growth retardation in these children.
Key Words: hemoglobin disorders, serum ferritin, thalassaemic children, chronic hypoxia.

INTRODUCTION

The inherited hemoglobin disorders are the most common single-gene defect in man. The frequency of the carrier state is estimated to be 270 million, with about 400,000 annual births a year of infants with serious hemoglobinopathies.

The prevalence of hemoglobinopathies is on the rise worldwide. This is a significant concern 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 the lack or decreased synthesis of either α or β globin chains of hemoglobin. It ends in ineffective erythropoiesis as well as lysis of mature red cells in the spleen.[2]

For Thalassemia optimal management, a multidisciplinary approach is essential involving pediatricians, transfusion specialists, endocrinologists, a child psychiatrist. Even in the best of the centers, the control of the disease is far from satisfaction.[3]

The only curative treatment of thalassemia is bone marrow or stem cell transplantation. This procedure is costly for a patient in developing countries like India. The backbone for the management of thalassemia is lifelong blood transfusion and iron chelation therapy.[4,5]
The government and non-governmental organizations, particularly when compared to the more significant health burden in our country, such as malnutrition, respiratory infection, diarrheal illness, & other infectious diseases, have not regarded thalassemia and other hemoglobinopathies as an essential public health problem.[6] Hence the thousands of children with this disease are incredibly precarious. From the aspects mentioned above, it would be clear that in developing nations like India, the prevention of Thalassemia will be a better option than cure.

AIMS AND OBJECTIVES

The present study was undertaken to
1) To assess the growth and development according to pretransfusion HB levels.
2) To determine the growth and development according to serum ferritin levels.

MATERIALS AND METHODS

Source of data: The present study was a hospital-based on a prospective observational study conducted in tertiary care hospital Kurnool. The total number of cases are 50.
Inclusion criteria: The children diagnosed to have Thalassemia major based on hemoglobin electrophoresis, came for blood transfusion, and who were advised to take Deferiprone are included in the study.

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 04, 2022

Exclusion criteria: The children had a severe systemic illness.

Method of collection of data:

1) 50 patients who are coming for blood transfusion and chelating therapy.

2) The serum ferritin level was estimated in transfusion-dependent thalassaemic children who had received more than 15 transfusions.

3) At each visit pre-transfusion, hemoglobin was analyzed by Sahli's method, and complete blood count was analyzed using a peripheral smear. At each visit, the child was thoroughly examined for adverse reactions.

4) Following anthropometric measurements were taken at hospital admission who came for blood transfusion.

- Height in cm, Weight in kg
- Mid arm circumference in 1-5 year children, sexual maturity.

5) Taken a detailed history of diagnosis, i.e. age of diagnosis, address, family history of consanguinity, pedigree chart, socioeconomic status.

Investigations done during the study period are the following:

1. HB, Complete blood picture.
2. RBC Indices, i.e., mcv, mchc, iron-binding capacity.
3. Peripheral smear, reticulocyte count.
4. Hemoglobin electrophoresis.
5. Serum ferritin levels.
6. Screening for HIV-1, 2, HBV, HCV, BY standard methods.

Ethical clearance: The study was approved by the ethical comity of Kurnool Medical College, Kurnool.

Statistical Methods: Chi-square and Fisher exact has been used to find the association of age and mean pre-transfusion HB% and mean ferritin levels with weight & height for age as per IAP standard.

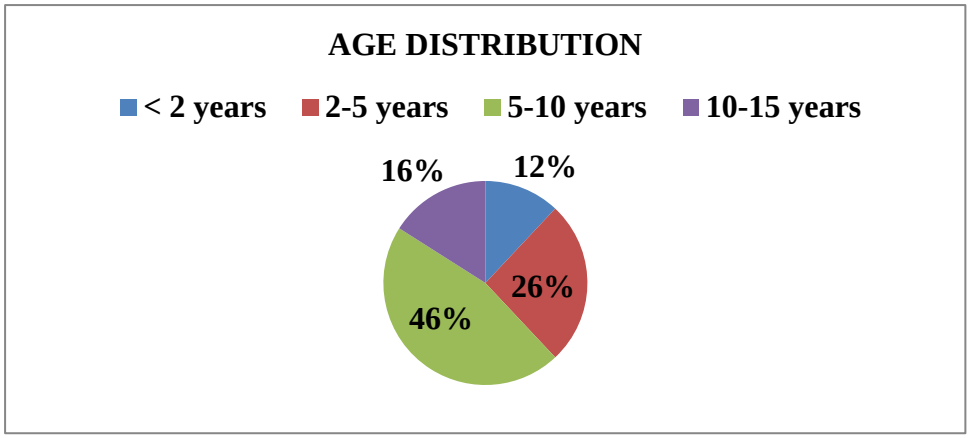
RESULTS

Table 1: Age Distribution among Sex Groups

AGE	FEMALE	MALE	TOTAL	PERCENTAGE
< 2 years	3	3	6	12
2-5 years	6	7	13	26
5-10 years	7	16	23	46
10-15 years	3	5	8	16
TOTAL	19	31	50	100 %

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 04, 2022

Graph 1: Age Distribution among Sex Groups

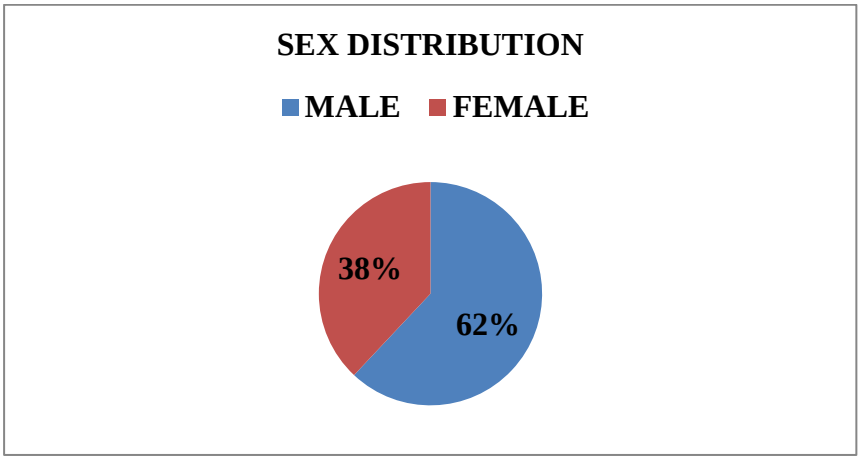


Nearly 60% of cases (31) were boys. Out of that, 3 cases in <2 years, 7 cases between 2-5 years, 16 cases in the age group of 5–10 years, and 5 cases in the age group of 10-15 years. 19 cases out of 50 were girls.

Table 2: Sex Distribution of 50 Cases

SEX	NUMBER	PERCENTAGE
MALE	31	62
FEMALE	19	38
TOTAL	50	100

Graph 2: Sex Distribution of 50 Cases



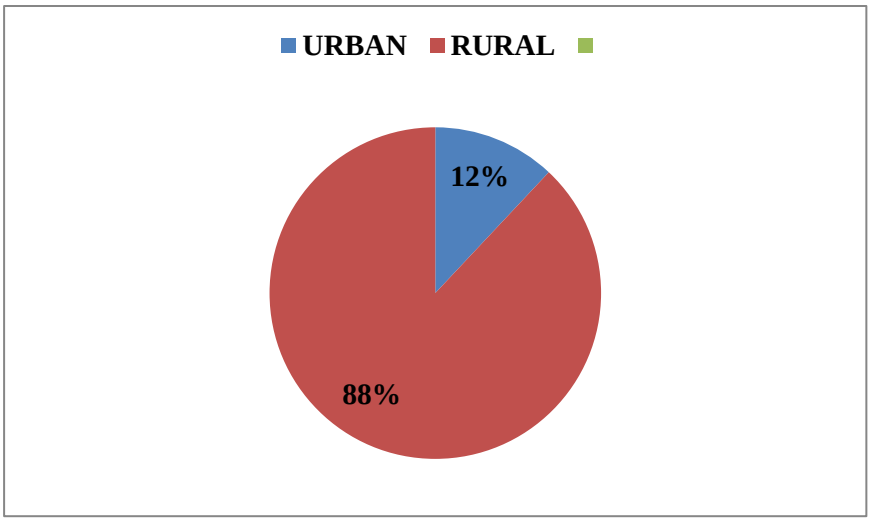
In the study on 50 thalassemia children, 62% were boys, and 38% were Girls.

Table 3: Shows Urban/ Rural Distribution in 50 Cases

REGION	NUMBER
URBAN	6
RURAL	44
ALL REGIONS	50

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 04, 2022

Graph 3: Regional Distribution

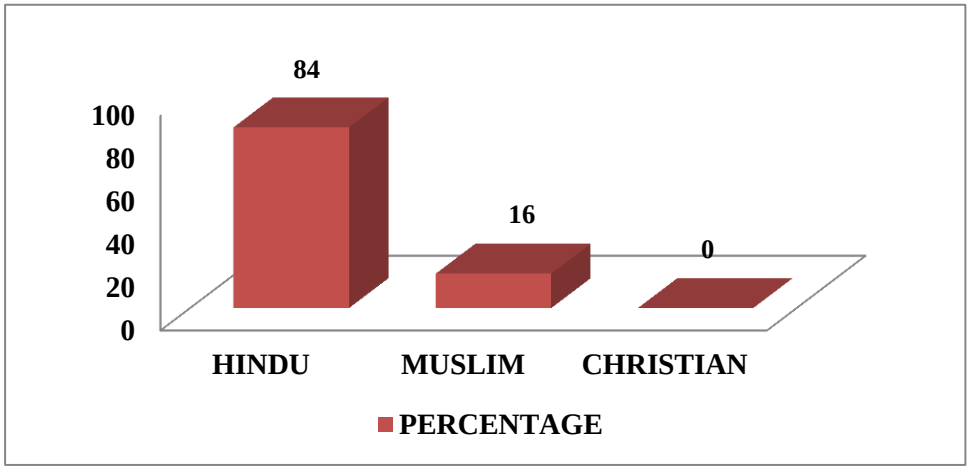


The urban/ rural distribution of 50 cases is shown in table 3. It is interesting to Note that 88% of cases were from rural areas, and nearly 12% of cases from urban areas.

Table 4: Distribution of Religion in 50 Cases

RELIGION	NUMBER	PERCENTAGE
HINDU	42	84
MUSLIM	8	16
CHRISTIAN	0	0
ALL RELIGIONS	50	100 %

Graph 4: Distribution of Religion Of 50 Cases



Distribution of 50 cases, according to religion, is shown in table 4. Nearly 84% of cases (42) were seen among Hindus; 16% cases (8) among Muslims and none among Christians.

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 04, 2022

Table 5: Age of Diagnosis In Thalassemia Major

AGE	AGE OF DIAGNOSIS IN MONTHS
MINIMUM AGE	3.6
MAXIMUM AGE	2.5
MEAN AGE	8.6

The mean age of diagnosis in Thalassemia Major was approximately 8.6 months. The minimum age of diagnosis was 3.6 months, and the maximum age of diagnosis was 2.5 years.

Graph 5: Age of Diagnosis In Thalassemia Major

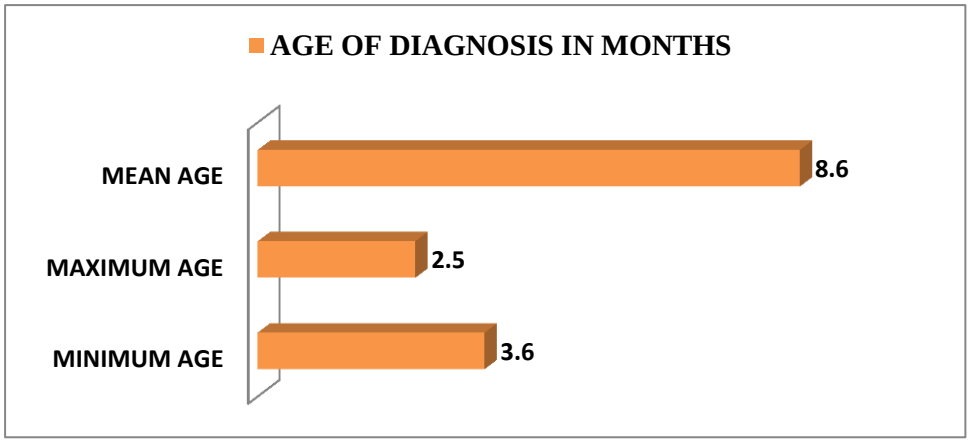


Table 6: Depicts Mean Mid-Arm Circumference In1-5-Year-Old Children

N	Range(cms)	Mean
19	11 - 13.5	12.01

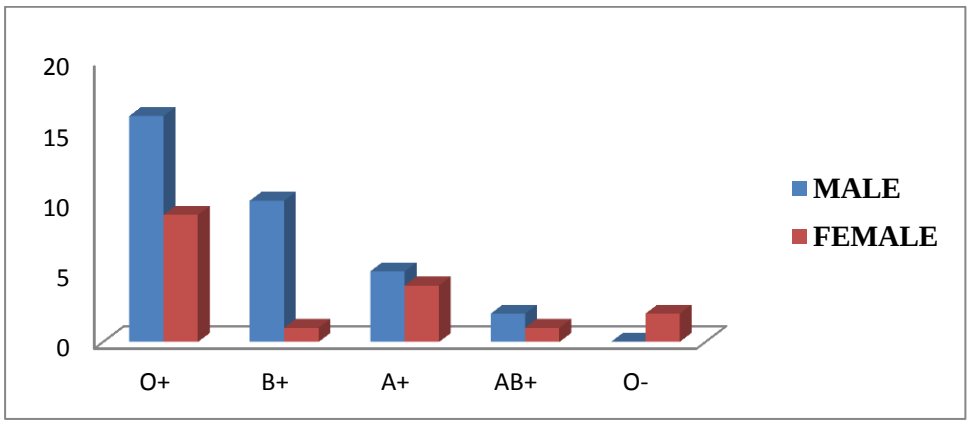
Mid arm circumference in the present study was 12.01 cms compared to 14.72 cm in the study of Anice George. Et al.[13], indicating inadequate nutrition.

Table 7: The Distribution of Blood Groups in 50 Cases

BLOOD GROUP	MALE	FEMALE
O+	16	9
B+	10	1
A+	5	4
AB+	2	1
O-	0	2
TOTAL	33	17

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 04, 2022

Graph 6: Distribution of Blood Groups in 33 Cases



The predominant blood group among 50 cases was O^{+ve} (25), followed by B^{+ve}(11).

Table 8: Depicts The Status of Iron Chelation Therapy

CHELATION THERAPY	NUMBER	PERCENTAGE
ON CHELATION	07	14%
IRREGULAR CHELATION	43	86%

The above table shows the status of iron chelation therapy in 50 cases. Only 14% (07cases) of 50 cases are on chelation therapy and the rest 86% (43 cases) are on irregular iron chelation therapy.

Graph 7: Status of Iron Chelation Therapy

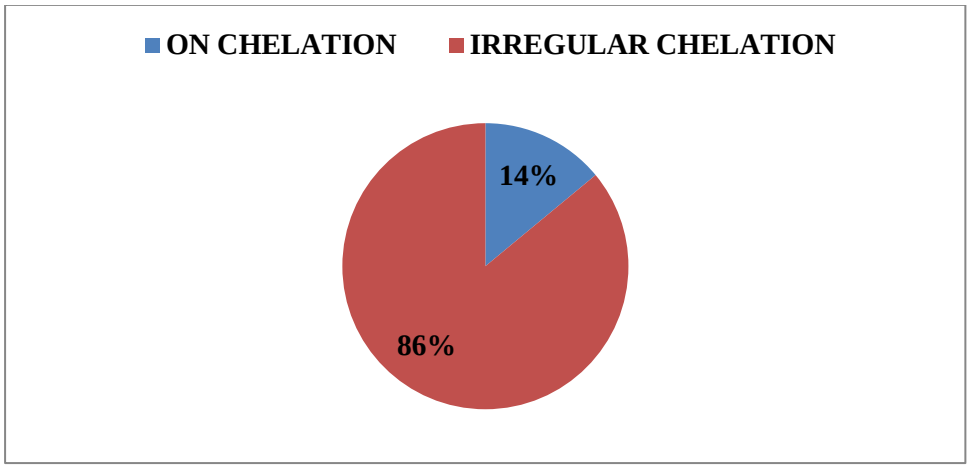


Table 9: Pre-Transfusion Hb Levels

PRE TRANSFUSTION HB LEVELS	NUMBER	PERCENTAGE
<6gm/dl	08	16

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 04, 2022

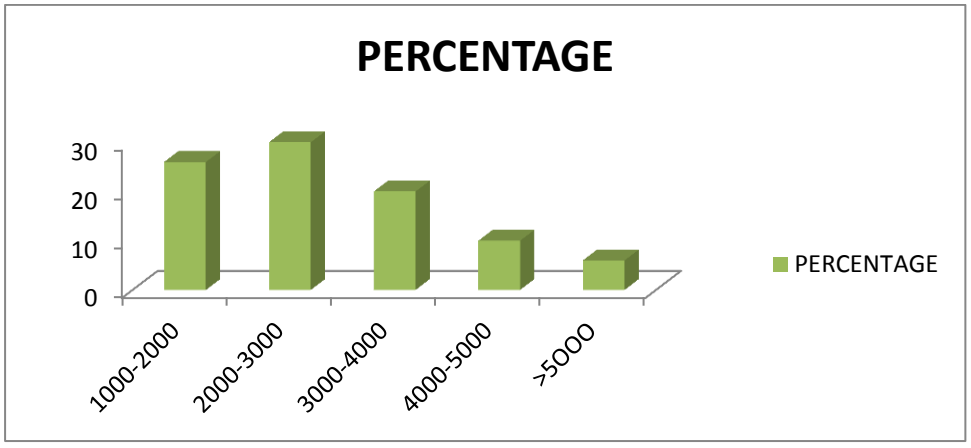
6-9gm-dl	36	72
>9gm/dl	06	12
Total	50	100%

The pre-transfusion hemoglobin of 36 cases was between 6 – 9 gm/dl in 72% of cases. 16% cases had levels less than 6 gm/dl, and only 12 % had pre-transfusion Hb levels above 9 gm/dl

Table 10: Serum Ferritin Levels in 50 Cases

SERUM FERRITIN LEVELS (ng/dl)	**NUMBER**	**PERCENTAGE**
<1000	04	8
1000-2000	13	26
2000-3000	15	30
3000-4000	10	20
4000-5000	05	10
>5OOO	03	6
TOTAL	50	100

Graph 9: Serum Ferritin Levels 50 Cases



Among the cases, it is very clearly shown that majority of the patients 30 % had ferritin levels 30% were in between 2000 to 3000 ng/dl, 26% between 1000 and 2000 ng/dl, 20% with values in between 3000 and 4000 ng/dl, 10% between 4000 and 5000 ng/dl, 8% < 1000ng/dl and 6% with toxic levels of above 5000 ng/dl. 92 % of patients had high ferritin levels requiring chelation therapy, indicating the importance of early identification of these cases, monitoring them, and institution of chelation therapy at the earliest. Towards the end, we feel that we should create awareness among medical practitioners about the early diagnosis of cases, provide facilities for hematological diagnosis and possibly

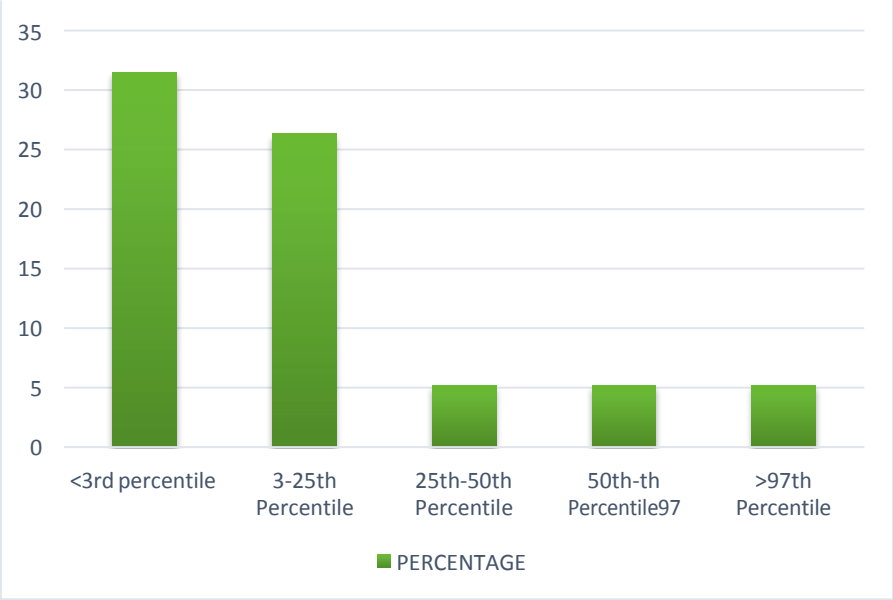
ISSN: 0975-3583,0976-2833 VOL13, ISSUE 04, 2022

carrier detection strategiesin India.

Table 11: Physical Growth Patterns (Weight for Age) Girls

WEIGHT FOR AGE	NUMBER	PERCENTAGE
<3rd PERCENTILE	06	31.5
3-25th PERCENTILE	06	31.5
25-50th PERCENTILE	05	26.3
50-97thPERCENTILE	01	5.2
>97th PERCENTILE	01	5.2
TOTAL	19	100

Graph 10: Physical Growth Patterns (Weight forAge), Girls



In the study, most of the cases (31.5%) were below the 3rd percentile, 31.5 %were between the 3rd to 25th percentile, followed by 26.3% between 25th – 50th percentile. Only a small fraction of 5.2% was above the 97th percentile.

Table 12: Physical Growth Patterns (Weight for Age)Boys

WEIGHT FOR AGE	NUMBER	PERCENTAGE
<3rd PERCENTILE	16	51.6
3-25th PERCENTILE	12	38.7
25-50th PERCENTILE	02	6.4

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 04, 2022

50-97thPERCENTILE	00	00
>97th PERCENTILE	01	3.2
TOTAL	31	100

In the study, most of the cases (51.6%) were below the 3rd percentile, 38.7 % werebetween 3rd to 25th percentile, followed by 6.4% between 25th – 50th percentile. Only a small fraction of 3.2% was above the 97th percentile.

Table 13: Depicts The Height For Age Distribution Among 50 Cases Boys

HEIGHT FOR AGE	NUMBER	PERCENTAGE
<3rd PERCENTILE	14	45.2
3-25th PERCENTILE	07	22.5
25-50th PERCENTILE	08	16.1
50-97th PERCENTILE	01	3.2
>97thPERCENTILE	01	3.2
TOTAL	31	100%

In our 50 cases of thalassemia, 45.2% were below the 3rd percentile; 22.5% were between the 3rd – 25th percentile; 16.1% between 25th-50th percentile; 3.2% between 50th-97th percentile and 3.2% were >97th percentile. The majority of thecases are <3rd percentile.

Table 14: Height For Age Distribution Among 50 Cases Girls

HEIGHT FOR AGE	NUMBER	PERCENTAGE
<3rd PERCENTILE	07	36.8
3-25th PERCENTILE	06	31.5
25-50th PERCENTILE	03	15.7
50-97th PERCENTILE	03	15.7
>97thPERCENTILE	01	5.2
TOTAL	19	100

In our 50 cases of thalassemia, 36.8% were below the 3rd percentile; 31.5% were between the 3rd – 25th percentile; 15.7% between 25th-50th percentile; 15.7% between 50th-97th percentile and 5.2% were >97th percentile. The majority of thecases are <3rd percentile.

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 04, 2022

Table 15: Depicts The BMI Distribution Among Boys

BMI IN PERCENTILE	NUMBER OF BOYS	PERCENTAGE
<3rd	9	29
5 to10th	2	08
10 to25th	7	24
3^{rd} to50th	4	12
25^{th} to50th	4	12
50th	0	00
50^{th} to 99th	4	12
OBESE	1	03

The majority of the cases (29%) among Boys were < 3^{rd} percentile and 0% at the 50^{th} percentile. The majority of the cases (26%) among girls were <3^{rd} – 50^{th} percentile and 0% atthe 5^{th} - 10^{th} percentile.

In our study pre-transfusion Hb levels < 6 gm (8) come under severely under- nourished and under-nourished. 6 - 9 gm (36) come under 3^{rd} - 50^{th} percentile. > 9 gm (6) come under 50^{th} - 97^{th} percentile. The chi-square value is 6.785 and P value is 0.03. Result is significant.

In our study among 50 cases, 19 members are with < 2754 serum ferritin levels and 31 are with > 2754 serum ferritin levels reflecting importance of regular chelationfor growth.

In our study, out of 18 cases, 10 cases were in 9-10 years age. 4 cases were in 11- 13 years of age and 4 cases were in 13-15 years of age. Out of 10 cases, in 9-10 years of age 9 cases showed SMR Stage 0 and 1 cases showed SMR Stage 1. Out of 4 cases, in 11-12 years, 2 cases were in SMR Stage 0 and 2 cases were in SMR Stage 1. Out of 4 cases, in 13-15 years of age 3 cases showed SMR Stage 1 and 1 case showed SMR Stage 2. All the cases having serum ferritin levels >2754. From the above information the inference is SMR is delayed in both males and females according to their age because most of the cases having pretransfusion Hb levels <9 gms and serum ferritin levels >2754 though this observation was not statistically significant. ($p = 0.9$).

DISCUSSION

The present study is a hospital-based prospective observational study of the growth pattern and serum ferritin levels in transfusion-dependent thalassemic children. The study aims to assess growth patterns and to assess the efficacy of Deferiprone in the reduction of iron overload in thalassemic children.

The age group of patients in the present study were between 1 to15 years, with the mean age being 7.00 ± 3.05 years, compared with other studies.

Our study correlates well with the other studies with respect to the religion distribution of thalassemia. However, it cannot be said that it is more common among Hindus as it is

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 04, 2022

proportional to the population (80%). The majority of children belong to rural setup, representing the population covered by the hospital.[7]

Mean age of diagnosis: The finding in the present study on age of diagnosis correlates with the study by Prieta et al. who observed 75.8% of cases were diagnosed below 2 years. Thalassemia major homozygous of the disease manifest very early in childhood with pallor being evident in the first year of life. In the present study, all the children manifested below 2-5 years.[8]

Blood group distribution: In the present study majority of children belong to O+ and B+ representing common blood groups.

Mean pre-transfusion hemoglobin level: The mean Pre transfusion hemoglobin level in the present study was 7.5 gm%. This is well below the recommended level of 9.5-10 gm% for the adequate growth of thalassemic children.[9]

All the children in the study had mean Pretransfusion hemoglobin of less than 8gm% compared to 8.6% percent of children in research conducted by Anice George et al., indicating inadequate transfusion.[10]

Most of the children in our study belong to the lower socio-economic class. Though blood transfusion and Deferiprone was given free of cost, many had difficulties in frequently coming to the hospital because of multiple factors like lack of funds for transportation, loss of daily wage for accompanying person, difficulty in getting frequent leave from school, etc.[11]

Normal growth of β-thal children during the first 10 years of life depends upon the maintenance of hemoglobin levels above 8.5 g/dl. During this period of the child's life, hypoxia may be the main factor retarding growth, and the maintenance of hemoglobin levels above 10-11g/dl together with adequate iron chelation therapy makes the β-thal patients indistinguishable from their non- thalassemic peers, indicating need to ensure regular blood transfusion.[12]

Out of 50 children, the majority had less weight and height (88% and 78%, respectively) compared to ICMR standards. This finding correlated well with the study of Anice George. Et al. 13 who observed that 68.7% and 71.2% of thalassemic children had less weight and height, respectively, when compared with the IAP study.[13]

These findings suggest that the majority of thalassemic children are growing at a lesser rate compared to healthy children.

The present study, as compared with the study of Anice George et al. -with the increasing age, more and more thalassemic children had growth retardation, weight being affected more than height. However, this finding was not significant in the present study.

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 04, 2022

Anthropometric observation in our study according to serum ferritin: In the present study out of 50, 19 are with < 2754 sr. Ferritin levels &weight for age <50% are 6,>50% are 13 and 31 with > 2754 sr. ferritin levels weight for age <50% are 18, >50% are 13.

The mean Pre transfusion hemoglobin level in the present study was 7.5 gm%. This is well below the recommended level of 9.5-10 gm % for te adequate growth of thalassemic children.

The present study, as observed in the study of Anice George et al., study retardation in weight and height was more in thalassemic children with less hemoglobin concentration; this observation is statistically significant in the present study.[14]

Retardation of various parameters at an early age is more likely to be secondary to chronic hypoxia following inadequate blood transfusion. Kattamis et al. observed that t he growth of thalassemic children during the first decade largely depends upon the maintenance of reasonably normal hemoglobin. This was also observed in the study, as evidenced by the positive correlation between hemoglobin levels and weight and height for age.

Mid arm circumference in the present study was 12.1 cms compared to 14.72 cm in the study of Anice George. Et al, indicating inadequate nutrition.

Sexual Maturity Rate: In our study, out of 50 cases, 18 cases are between 9-15 years of age and all cases have delayed SMR who are not maintaining mean Hb and high Sr. ferritin levels. Present study correlated with MDC Borgna- pignatti et al. 1985 study.[15]

CONCLUSION

Thalassemia syndromes are a significant cause of morbidity and mortality in children. Most of the children had mean pretransfusion hemoglobin of less than 8 gm%, mean being 7.5 gm%, indicating inadequate blood transfusion. Growth retardation was a significant problem in thalassaemic children. The number of children with growth retardation increased with increasing age and decreasing hemoglobin percentage, indicating chronic hypoxia may be responsible for the growth retardation in these children. SMR is delayed in both males and females according to their age because most of the cases having pretransfusion HB levels < 9 gms and sr. Ferritin levels >2754.

REFERENCES

1. Sarnaik SA. Thalassemia and Related Hemoglobinopathies.Indian J Paediatric 2005; 72:319-324.
2. Kumar V. Disease of red cells and bleeding disorders. In: Robbins textbook of pathology basis of disease, 5th edn.Cothran RS, Kumar V, and Robbins SL. India: WB Saunders, 1994, 583-627.
3. Quirolo Keith and Elliot Vichinsky. Thalassemia syndromes. In: Nelson Textbook of Pediatrics, 17th edn. Behrman RE, Kliegman RM, and Jenson HB (eds). India. Elsevier, 2004, 1630-34.
4. 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.
5. Weatherall DJ. Common genetic disorders of the red cell and the "malaria hypothesis" Annals of TropicalMedicine Parasitology 1987; 81:539-548.

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 04, 2022

6. Lokeshwar M.R, Mamta Manglani, Nitin Shaw, Swathi Kanakia: Modern trends in the management of Thalassemia, Indian journal of practical Pediatrics1997;5:287- 295.
7. Choudhry V.P, Desai. N Pati H.P, Nanu. A: Current Management of homozygous ß Thalassemia, Indian pediatrics 1991;28:1221-29.
8. 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.
9. Cooley TB, Lee P. A series of cases of splenomegaly in children with anemia and peculiar bone changes. Trans Am Pediatr Soc 1925; 37:29-30.
10. Whipple GH, Bradford WL. Mediterranean disease – thalassemia (Erythroblastic anemia of Cooley): associated pigment abnormalities are simulating hemochromatosis. Journal of Paediatrics 1936; 9:279-311.
11. Gomber Sunil, Rohit Saxena, Nishi Madan. Comparative efficacy of Desferrioxamine, Deferiprone, and in combination with Iron Chelation in Thalassemic Children. Indian pediatrics 2004;41:21-26.
12. Verma IC, Choudhry VP, and Jain PK. Prevention of thalassemia. A necessity in India. Indian journal of pediatrics 1992;59:649-654.
13. George Anice, Aparna Bhaduri, Siddarth Sen, and Choudhry VP. Physical growth parameters in thalassemic children. Indian J Pediatrics 1997;64:861-871.
14. Barrs et ai 1974, Liver iron levels controlled by desferroxamine.
15. Agarwal M.B, et al. Long term assessment of efficacy and safety of L 1, an oral iron chelator, in transfusion-dependent thalassemia: Indian trial. British journal hematology.1992;82:460-66.