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Dr. Bushra Nasreen
Assistant Professor,
Department of Paediatrics,
VRK Womens Medical College, Teaching Hospital and Research Centre, Hyderabad, Telangana, India

Corresponding Author:
Dr. Bushra Nasreen
Assistant Professor,
Department of Paediatrics,
VRK Womens Medical College, Teaching Hospital and Research Centre, Hyderabad, Telangana, India

A prospective study on growth pattern and effect of serum ferritin, haemoglobin levels on physical growth in thalassemic childern

Dr. Bushra Nasreen

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Abstract
Background: Thalassemia major is one of the most common genetically transmitted diseases in the world and is associated with reduced synthesis of structurally normal hemoglobin. ß-thalassemia is an autosomal recessive single gene disorder. Keeping this in mind, present study was undertaken to study the growth pattern of transfusion dependent thalassaemic children and to assess the effect serum ferritin, haemoglobin levels on physical growth pattern in thalassemic children.
Methods: A prospective observational study was done on 52 thalassaemic patients (aged 2 years-12 years) who attended Department of Pediatrics. Anthropometric measurements like weight and height were taken from all patients. Sexual maturity rating was done in girls ≥10 years and boys≥11 years. Lab parameters included pre-transfusion hemoglobin (Hb) and serum ferritin. Percentiles for weight, height and body mass index were calculated using WHO (2007) reference data.
Results: Among 52 transfusion dependent thalassemic children majority i.e. 35(67.3%) were more than 6years.Mean age was 8 ± 3.05. Majority of children i.e. 32(61.6%) were male. Mean age of diagnosis was 9.2 months, youngest case being diagnosed at 3rd month, and oldest being at 20 months. Among 52 children most of them are born to non-consanguineous couple. Majority of the children had pre-transfusion haemoglobin in the range of 5-7 gm%. Among 52 children 61.6 % (n=32) had mean serum ferritin more than 2500, and 38.4% (n=20) had mean serum ferritin value less than 2500. The present results showed that, Among 52 children according to IAP standards weight for age less than 50th percentile was 86.5% (n=45) and more than 50th percentile was 13.5%(n=7). Among 45(86.5%) children who had less than 50th percentile weight for age, 19.2 % (n=10) children were less than 6 years of age, remaining 67.3% (n=35) children belongs to 7 to 12 years of age. Among weight for age <50th percentile children, 82.2% of children had mean pre transfusion haemoglobin<7gm%.
Among height for age <50th percentile children, 91.1% of children had mean pre transfusion haemoglobin<7gm%. In the present study we found that, Among weight for age <50th percentile children, 75.5% of children had mean serum ferritin >25oong/ml. Among height for age <50th percentile children, 76.4% of children had mean serum ferritin >2500ng/ml.
Conclusions: Regular blood transfusion with growth monitoring and appropriate iron chelation (Sr. Ferritin >1000 ng/ml) is of utmost importance in transfusion dependent thalassaemic children.

Keywords: thalassemic, ferritin, haemoglobin and hemoglobinopathies

Introduction
Thalassemias are a group of hereditary anemia's resulting from defects in haemoglobin production. They are the world's most common monogenic disorders. 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 hemoglobinopathies. The prevalence of hemoglobinopathies is on the rise worldwide. This is of special importance in developing countries, where it increases the burden of health care delivery systems [1].
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 [3-5]. It has been estimated that over 6000-8000 children, who are homozygotes of β-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 [6].

In India, the awareness of thalassemia is limited and the diagnosis of thalassemia is often delayed and is only possible at major institutions. Blood transfusion, though a well established form of therapy, is not available to the majority of thalassemics because of its limited availability.
Patients often have to travel for off distances for a unit of blood, to thalassemic units where facilities for regular transfusions are available. There are only a few thalassemia units where these children are regularly given blood transfusion and monitored for various parameters.
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 [7].
The combination of regular blood transfusions and chelation therapy has increased the life expectancy of thalassemics into 4th & 5th decades of life. On the other hand, frequent blood transfusion has lead to iron overload with many complications the commonest of which is growth failure [8].
The etiological factors leading to growth retardation in transfusion-dependent thalassemia are varied; with chronic anemia and iron overload induced endocrinopathies having been implicated in this complication. A close monitoring of growth may lead to early identification and treatment of these complications to ensure that patients achieve near normal adult height.
There are very few studies available on the growth parameters and factors affecting growth in thalassemic children from this region. Thus, this study was undertaken to assess the physical growth in thalassemic children in relation to the iron stores and haemoglobin level.

Materials and Methods

Study setting: The present study is a hospital based prospective observational study, done at, department of Pediatrics, Dr V.R.K. Women's Medical College from during the year Jan 2017-June 2018

Study period: Study was conducted 18 months from the time of approval of institutional ethics committee.

Inclusion criteria

All children diagnosed of beta thalassemia major by Hb electrophoresis registered in thalasemia clinic, aged between 2-12 yrs on blood transfusion.

Exclusion criteria

1. The children who were having severe systemic illness.
2. The children whose parents have not given consent.
3. Method of collection of data

Data collection was done after obtaining consent from parents by a standard proforma. Detailed history was taken giving more importance to age at diagnosis, consanguity, family history. At each visit children were examined clinically for any other systemic illness. At each visit pre transfusion haemoglobin was analyzed by Sahlis method and complete blood counts were analyzed using peripheral smear.
Serum ferritin levels were estimated at the beginning of the study, at 3rdmonth, 6th month and at 9th month. Blood samples were collected by drawing 2ml of blood from cubital vein, into sterile vacuum tubes and stored in refrigerator till it was transported to the laboratory. Serum ferritin was analyzed using MAGIWEL KIT by solid phase enzyme-linked immunosorbant assay (ELISA) - A quantitative assay.
Detailed physical examination was done and the following parameters were recorded at every visit, Weight in kilograms measured by digital weighing scale. Standing height in centimetres measured by stadiometre. Obtained parametres were plotted on the IAP growth charts for the age and sex.

Statistical Methods: Chi-square and Fisher exact test has been used to find the association between mean pre transfusion haemoglobin, mean ferritin with weight for age and height for age as per the IAP growth charts.

Statistical software: The Statistical software namely SPSS 11.0 and Systat 8.0 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

Results

Table 1: Age and sex distribution of the study

Age	Female (%)	Male (%)	Total (%)
≤6 yrs	6 (11.5%)	11 (21.2%)	17 (32.7%)
7-12 yrs	14 (26.9%)	21 (40.4%)	35 (67.3%)

Among 52 transfusion dependent thalassemic children majority i.e. 35(67.3%) were more than 6years.Mean age was 8 ± 3.05. Majority of children i.e. 32(61.6%) were male.

Table 2: Mean Age of diagnosis

Minimum age	3 months
Maximum Age	9 months
Mean	9.2 months

Mean age of diagnosis was 9.2 months, youngest case being diagnosed at 3rd month, and oldest being at 20 months.

Table 3: Distribution of Blood group

Blood group	Number	Percentage
A^+ VE	14	26.9
A^-VE	0	0
O^+VE	15	28.8
O^-VE	0	0
B^+VE	20	38.4
B^-VE	0	0
AB $^+$VE	3	5.7
AB $^-$VE	0	0

Table 4: Parental Consanguinity

Consanguinity	Number
First degree	00
Second degree	06
Third degree	12
Fourth degree	04
Non-consanguinity	30

Among 52 children most of them are born to non-consanguineous couple, 12 children born to third degree consanguineous couple, 6 children were born to second degree consanguineous couple and 4 were born to fourth degree consanguineous couple.

Table 5: Mean transfusion of pre hemoglobin

Mean pre transfusion	Number	%
≤7gm %	37	71.1
7.1-10 gm %	15	28.8
< 10 gm%	00	0.00
Mean±SD	6.62±1.20	

All children in the present study had mean pre-transfusion haemoglobin less than 10 gm% during the study period. Average pre-transfusion haemoglobin during study period ranged from 5 to 7 gm % with mean being 6.6 ± 1.204. Majority of the children had pre-transfusion haemoglobin in the range of 5-7 gm%.

Table 6: Mean serum ferritin concentration (ng/ml)

Serum Ferritin	Number	Percentage
<2500 ng/dl	20	38.4
>2500 ng/dl	32	61.6
Mean±SD	28.99±65.68	

Among 52 children 61.6 % (n=32) had mean serum ferritin more than 2500, and 38.4% (n=20) had mean serum ferritin value less than 2500. Standard deviation is 2899 ± 656.848 Standard error of mean is 91.977. 95% confidence interval is between 2719.61 to 3080.15.

Anthropometry

Table 7: Weight for age

Weight for age according to IAP	Number	Percentage
Less than 50th percentile	45	86.5
More than 50th percentile	07	13.5
Total	52	100

Among 52 children according to IAP standards weight for age less than 50th percentile was 86.5 % (n=45) and more than 50th percentile was 13.5 % (n=7).

Table 8: Weight for age according to age wise

Age	Less than 50 than percentile	More than 50th percentile	Total
< 6yrs	10 (19.2%)	7 (13.5%)	17(32.7%)
7-12 yrs	35 (67.3%)	00	35(67.3%)
Total	45 (86.5%)	7 (13.5%)	52(100%)

Among 45(86.5%) children who had less than 50th percentile weight for age, 19.2 % (n=10) children were less than 6 years of age, remaining 67.3 % (n=35) children belongs to 7 to 12 years of age.

Table 9: Height for Age

Age	Less than 50th percentile	More than 50th percentile	Total
< 6yrs	4 (7.7%)	13 (25%)	17 (32.7%)
7-12 yrs	30 (57.7%)	5(9.6%)	35 (67.3%)
Total	34 (65.4%)	18 (34.6%)	52(100%)

Among 34 children who had height for age less than 50th percentile 7.7 % (n=4) children were belongs to less than 6 years of age and remaining 57.7 % (n=30) belongs to 7-12 years of age.

Table 10: Mean pre-transfusion haemoglobin and weight for age

Mean transfusion Haemoglobin	Less than 50th percentile		More than 50th percentile		Total
	< 6yrs	7-12 yrs	< 6yrs	7-12yrs	
< 7 gm %	10(19.2%)	27(52%)	0	0	37
7-10gm %	00	8(15.4%)	7(35%)	0	15

Among 45 children who had weight for age less than 50th percentile 37 children had mean pre transfusion haemoglobin <7 gm%. P-value for above observations is, 0.001. Chi square equals 16.148 with one degree of freedom.

Table 11: Mean pre-transfusion haemoglobin and height for age

Mean transfusion Haemoglobin	Less than 50th percentile		More than 50th percentile		Total
	< 6yrs	7-12 yrs	< 6yrs	7-12 yrs	
< 7 gm %	4(7.6%)	25(51.9%)	6(11.5%)	0	37
7-10gm %	00	3(5.7%)	7(13.44%)	5(9.6%)	15

Among 34 children who had height for age less than 50th percentile 30 children had mean pre transfusion haemoglobin <7gm%. P-value for above observations is 0.001

Table 12: Mean ferritin with weight for age

Mean ferritin	Less than 50th percentile	More than 50th percentile	Total
<2500 ng/dl	11(21.1%)	5(9.6%)	16
>2500 ng/dl	34(65.4%)	2(3.8)	36

Among 45 children who had weight for age less than 50th percentile according to IAP standards, 34 children had mean serum ferritin more than 2500 ng/ml and remaining 11 children had mean ferritin <2500. P-value for above observations equals 0.0228.

Table 13: Mean ferritin with height for age

Mean ferritin	Less than 50th percentile	More than 50th percentile	Total
<2500 ng/dl	8 (15.4%)	8 (15.4%)	16
>2500 ng/dl	26 (50%)	10 (19.2%)	36

Among 34 children who had height for age less than 50th percentile26 children had mean serum ferritin more than 2500 ng/ml. Among 18 children who had height for age more than 50th percentile, 10 children had mean serum ferritin more than 2500 ng/ml. P-value for above observations equals to 0.2056.

Discussion

The combination of regular blood transfusions and chelation therapy has increased the life expectancy of thalassemics into 4th & 5th decades of life. On the other hand, frequent blood transfusion lead to iron overload with many complications the commonest of which is growth failure. Growth disturbances are also a major clinical feature of untreated patients with thalassemia.

The etiological factors leading to growth retardation in transfusion dependent thalassemic children are varied, with chronic anemia and iron overload-induced endocrinopathies.

A close monitoring of growth may lead to early identification and treatment of these complications to ensure that patients achieve near normal adult height.

There are very few studies available on the growth parameters and factors affecting growth in thalassemic children from this region. Thus, this study was undertaken to assess the physical growth in thalassemic children in relation to the iron stores and hemoglobin levels.

The present study is a hospital based prospective study conducted in the, Dept. of Pediatrics, Dr V.R.K. Womens Medical College.

Present study was conducted among 52 children diagnosed to have beta thalassemia major by Hb electrophoresis.

Age and sex distribution

52 children were belongs to age group between 2 to 12 years. Thalassemia major homozygous of the disease manifest very early in childhood with pallor being obvious within the first year of life. Among 52 children youngest age at which thalassemia was diagnosed was 3months, and oldest being 20 months, mean age of diagnosis was9.2 months. Above finding was correlated with study by *Prita et al* who observed 75.8%of cases were diagnosed below 2 years and higher when compared to study from Nadkarni A *et al, Mumbai* [8] where the mean age of diagnosis was 5 months. Among 52 children 67.3% children had more than 7 years of age which is similar to study done at *malik et al, kolkata* [9] and *sangani et al Mumbai* [10]. Similarly in a study from 12 reference hospitals in North America 11 show increasing mean ages of thalassaemia major patients from 6.2 to 16.7 in 2 decades.

Among 52 children, 32 children were males, 20 children were females. When compared to *V.P Choudhry et al.,* [12] *Anice George et al.* [13] study male and female distribution almost similar. In one study conducted by *Rai ME et al.,* [14] males were 70%.Even though thalassemia is an autosomal recessive disorder, it should be equally distributed in both sexes but higher proportion is seen in males.

Consanguinity

Thalassemia being autosomal recessive disorder consanguinity should be present in large number of cases. However it is interesting to see that 57.6% of cases there was no obvious consanguinity. The inbreeding is being practiced in India for more than 2000 years and is so much common varying from 25– 50% in different Southern states of India15. When inbreeding is so common and so long practiced, the true division between consanguineous and non-consanguineous becomes obscured, and hence even though there is no apparent consanguinity, sharing of genes might have occurred. If we draw a extended pedigree chart then we might find the relation between consanguinity and non-consanguinity.

Blood group distribution

In the present study majority of children, belong to blood group B^+ and O^+ representing common blood group prevalent in the population.

Physical growth

Anice George et al., [13] did a study on growth parameters of 233 thalassemic children and were compared with non-thalassemic siblings, according to *Anice George et al.,* [13] growth was effected in thalassemic children. *Anice George et al.,* [13] study showed 68.7% of children had weight for age less than 50th percentile according to ICMR standards. In present study 86.5% of children had weight for age less than 50thpercentile, similar to *Anice George et al* [13].

Anice George et al., [13] study showed 71.2% children had height for age less than 50th percentile according to ICMR standards. In present study 65.4% children had height less than 50th percentile. *Anice George et al.,* [13] divided children into two groups; one group belongs to less than 6years of age and another group more than 6 years of age.

Among these two groups children less than 6 years of age, 32.8% children had weight less than 50th percentile and in more than 6 years of age 74% children had weight less than 50^{th} percentile.

Present study showed 58.8% (10 in 17 children) of children among less than 6years of age had weight less than 50th percentile, where as all 35 children between 7-12 years of age group had weight for age less than 50th percentile.

Both studies showed weight for age was more affected after the age of 6years. According to *Anicegeorge et al* [13] study among 233 children 71.2% children had height for age less than 50th percentile.

Present study showed 65.4% children had height for age less than 50th percentile. In *Anice George et al* [13] study among age groups 42.2% children in less than 6years of age group had height less than 50 thpercentile, where as in more than 6 years of age group 75% of children had height less than 50th percentile.

In present study, 23.5% children belongs to less than 6 years of age group had height for age less than 50thpercentile, where as 85.7% children between age group 7-12 years had height for age less than 50th percentile.

The present study as comparable with the study of *Anice George et al.* [13] with the increasing age, more and more thalassemic children had growth retardation, weight being affected more than height. Other study done on 231 thalassemic children showed 46% had growth failure, present study also showed similar results [16].

Mean pre-transfusion haemoglobin level

Mean Pre transfusion haemoglobin level in the present study was 6.62gm%. This is well below the recommended level of 9.5-10 gm% for adequate growth of thalassemic children.

71.1% children in the study had mean pre-transfusion haemoglobin of less than 7gm% compared to 44.2 percent of children in study conducted by *Anice George et al.,* [13] have mean pre transfusion haemoglobin <8gm% indicating inadequate transfusion.

Most of the children in present study belong to lower socio economic class. Though blood transfusion was given free of cost, many had difficulties in coming frequently to hospital because of multiple factors like, poverty, lack of funds for transportation, loss of daily wage for accompanying person, ignorance, literacy.

Normal growth of β-thalassemia children during the first 10 years of life depends upon the maintenance of haemoglobin 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 haemoglobin levels above10-11g/dl together with adequate iron chelation therapy makes the β-thalassemia patients indistinguishable from their non-thalassemic peers, indicating need to ensure regular blood transfusion.

All children in the present study had mean pre transfusion

haemoglobin less than 10 gm% during the study period. Average pre-transfusion haemoglobin during study period ranged from 5 to 7 gm % with mean being 6.6 ± 1.20. Majority of the children had pre-transfusion haemoglobin in the range of 5-7 gm%.

Present study was similar to *Shivasankara et al.,* [17] study, *Fakher R et al.,* [18] study showing mean pre-transfusion haemoglobin as 6.66. Among 45 children who had weight for age less than 50th percentile 82.2 % (n=37), had mean pre-transfusion haemoglobin less than 7gm%.

According to *Anice George et al.,* [13] in which among children who had weight for age less than 50th percentile 82.5 % children had mean pre transfusion haemoglobin of less than 8gm%. present study was comparable to *Anice George et al* study. P value for present study is <0.01 which is statistically significant [13].

Among 34 children who had height for age less than 50th percentile, 91.1% children had mean pre-transfusion haemoglobin has ≤7gm%.

According to *Anice George et al* [13]study among children who had height for age less than 50th percentile, 77.7% children had mean pre transfusion haemoglobin ≤8 gm%. Present study was comparable to *Anice George et al* study. P value for present study was <0.01 which is statistically significant [13].

Above findings suggest that growth retardation might have been secondary to chronic hypoxia as growth retardation and it was more seen in children who had mean pre transfusion haemoglobin <7gm%.

Growth retardation in early age is more likely to be secondary to chronic hypoxia following inadequate blood transfusion. *Kattamis et al.* [19] observed that growth of thalassemic children during the first decade of life mostly depends upon maintenance of near normal hemoglobin. This was also observed in the study as evidenced by the positive correlation between haemoglobin and weight and height forage.

This indicates chronic hypoxia is not a contributing factor in properly treated children. Linear growth in childhood is disrupted only in a small percentage of children due to anemia, ineffective erythropoiesis and iron overload. During the first decade of life the maintenance of haemoglobin levels above 9 gm/dl together with adequate iron chelation therapy makes the children with thalassemia indistinguishable from their non thalassemicpeers20.

In *Harish K Pende et al* study, 1/3rd of children had weight for age less than <50th percentile who had more than 3000ng/ml serum ferritin [21]. In present study among 36 children who had serum ferritin >2500, 34 children had weight for age less than 50th percentile (94.4 %).It is high when compared to *Harish K Pande et al* study. P value for above observations showed 0.0228, so the results are moderately stastically significant. Among 36 children who had more than 2500 ng/ml serum ferritin 26 (72.2%) children had height for age less than 50th percentile. P value for above observations showed 0.2056 indicating above results are stastically insignificant.

In a study conducted in Israel, among 39 children, mean serum ferritin level during the study period was 2698 ± 1444 ng/mL. and short stature was found in 36% of patients who reached final height. Mean ferritin level of 2500 ng/mL during puberty was the cut-off for hypogonadism, and ferritin level of 3000 ng/mL during pre-puberty was the cut-off for final short stature. The authors concluded that high serum ferritin levels during puberty are a risk factor for hypogonadism, and high serum ferritin levels during the first decade of life predict final short stature 22.

Limitations

- Present study was conducted among 52 thalassemic children, if the number of children participated is more results will be more significant.
- Most of the children in present study belong to low socio economic class, hence growth pattern may be affected by low socio economic status.
- Because of illiteracy and ignorance some parents did not come to regular follow-ups.
- Many of the children who participated in present study were on chelation therapy, but most of them had poor compliance. So the effect of chelation therapy might be there on physical growth.

Conclusions

Thalassemia is one of the major causes of morbidity in children in India. It is also causing economical burden for family and society. Some of the parents are still feeling that it is a curse, and ignorant regarding the disease. Some of the parents were not bringing the children for regular blood transfusions and not on regular chelation therapy because of various reasons majority could be low socio economic status. Growth retardation was significant problem in thalassemic children. Mean pre transfusion haemoglobin levels were not according to guidelines. Number of children with growth retardation was increasing because of decrease in mean pre transfusion haemoglobin percentage and indicates chronic hypoxia may be responsible for the growth retardation in these children. Number of children with growth retardation was increasing with increasing age, indicates iron overload induced endocrinopathies.

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Conflict Of Interest

The authors declare that, they have no conflict of interest.

References

1. Sarnaik SA. Thalassemia and Related Hemoglobinopathies. Indian J Paediatric 2005; 72:319-324.
2. Michael R. De Baun, Melissa J. Frei-Jones,and Elliot Vichinsky. Thalassemia syndromes. In:Nelson's text book of paediatrics,20th ed. new delhi: saunders, 2016.
3. Weatherall DJ. The thalassemias. In: Stamatoyannopoulos G, Nienhuis AW, MajerusPH, 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. Lokeshwar MR, Mamta Manglani, Nitin Shaw, Swathi Kanakia: Modern trends in the management of Thalassemia, Indian journal of practical Pediatrics. 1997; 5:287-295.
6. Choudhry VP, Desai N, Pati HP, Nanu A. Current Management of homozygous βThalassemia, Indian

paediatrics. 1991; 28:1221-29.
7. Choudhry VP, Kashyap R, Acharya SK, Tandon N, Saxena A. Challenges in the Management of Thalassaemia, Mediquest Medical Information series. 1997; 15(3):1-9.
8. Nadkarni A, Gorakshakar AC, Lu CU, Krishnamoorthy R, Ghosh K, Colah R, Mohanty D. Molecular Pathogenesis and Clinical Variability of b-Thalassemia Syndromes Among Indians. Am J Hematol. 2001; 68:75-80.
9. Mallik S, Chatterjee C, Mandal PK, Sardar JC, Ghosh P, Manna N. Expenditure to Treat Thalassaemia: An Experience at a Tertiary Care Hospital in India. Iranian J Publ Health. 2010; 39 (1):78-84.
10. Sangani B, Sukumaran PK, Mahadik C. Thalassaemia in Bombay: Role of medical genetics in developing countries. Bulletin. 1990; 68(1):75-81.
11. Pearson HA, Cohen AR, Jane V. Giardina, Haig H, Kazazian Jr. The Changing Profile Homozygous Thalassemia: Demography, Ethnicity, and Current North American and Changes in Two Decades. Paediatrics. 1996; 97(3):352-6.
12. Choudhry VP *et al.* Deferiprone, efficacy and safety. Indian journal of paediatrics. 2004; 71:213-216
13. George Anice, Aparna Bhaduri, Siddarth Sen, Choudhry VP. Physical growth parameters in thalassemic children. Indian J Pediatrics. 1997; 64:861-871.
14. Rai ME, Tanoli ZM, Gandapur ASK. Clinical spectrum of patients of beta thalassemia: a review of fifty four patients. Glomal J Medical sciences. 2005; 3(2):55-60
15. Sastri KAN. A history of South India from prehistorical times to fall of vijayanagar. Madras: Oxford university press, 1955.
16. Kirti Grow, Pankaj Abrol, Minakshi Vashist, Ritu Yadav, Shiksha Sharma. Associated Complications In Beta Thalassemia Patients. IOSR Journal of Pharmacy. 2013; 3(1):22-25.
17. Shivashankara AR, Jailkhani R, Kini A. Hemoglobinopathies in Dharwad, North Karnataka: A hospital based study. Journal of clinical and diagnostic research. 2008; 2:593-599.
18. Fakir R. Microcytic hypochromic anemia patients with thalassemia: Genotyping approach. Indian J Med Science. 2009; 63(3):101-108.
19. Bhavana Singhal, Neha Shama, Ranjana Mathur. Iron overload and growth of thalassemic patients in Marwarregion. IJPSR. 2012; 3(7):2043-2049.
20. Soliman AT, El Zalabany MM, Amer M, Ansari BM. Growth and pubertal development in transfusion-dependent children and adolescents with thalassaemia major. Hemoglobin. 2009; 33:16-20.
21. 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.
22. Shalitin S, Carmi D, Weintrob N, Phillip M, Miskin H, Kornreich L, Zilber R, Yaniv I, Tamary H. Serum ferritin level as a predictor of impaired growth and puberty in thalassemia major patients. Eur J Haematol. 2005; 74:93-100.