Original Research Paper

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A CLINICO-EPIDEMIOLOGICAL STUDY OF THALASSEMIA IN TRANSFUSION DEPENDANT B THALASSEMIA CHILDREN AGED 2 TO18 YEARS ATTENDING TRANSFUSION CENTRE IN DISTRICT HOSPITAL, ELURU,WEST GODAVARI DISTRICT

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ABSTRACT

BACKGROUND: Thalassemia syndromes are caused by inherited mutations that decrease the synthesis of either α or β globin chains of haemoglobin. Imbalance in globin chain synthesis results in anaemia, tissue hypoxia, and red cellhemolysis.[1] In India, it is the most common single-gene disorder. Recent data indicate that about 7 % of the world's population is a carrier of a haemoglobin disorder, and that 300,000 - 500,000 children are born each year with the severe homozygous state of the disease worldwide.[2]

OBJECTIVE: To evaluate the socio-demographic factors growth parameters and analyse them with serum ferritin, average pretransfusion Hb, serum vitamin D3in the transfusion dependent β-Thalassemia in children between 2-18 years of age attending a transfusion centre in Eluru.

METHODOLOGY: This is a cross-sectional observational study in 77 Children between 2-18 years of age with transfusion dependent β-Thalassemia who are attending to a transfusion centre Eluru town. Detailed history was collected by predetermined questionnaire including Socio-demographic factors, anthropometric parameters and these are analysed along with average serum ferritin levels, average pre-transfusion Hb and serum vitamin D3 levels.

RESULTS: In the present study male (62.3%) were more than female (37.7%).Age at diagnosis was more in 0 to 6 months(66.2%)than 6 to 12 months(23.4%) and >12 months(10.4%). Children with carriers in the family were (51.9%) found to be more than those without carriers (48.1%) in the family. Means of serum ferritin, vitaminD3, average pre-transfusion Hb against z-scores of height, weight and BMI showed uniform distribution.

CONCLUSION: In our present study socio demographic factors and Anthropometric measurements grouped as z-scores are assessed with means of the three investigations (serum ferritin, vitaminD3, average pretransfusion Hb) and found uniform distribution. Growth retardation was noted in several children despite regular transfusions and chelation therapy. The causes of this need a thorough evaluation in a larger study. We did find a strong correlation between average ferritin levels and hepatomegaly in these children.

KEYWORDS : β Thalassemia, Thalassemia Major, Anthropometry, Serum Ferritin, VitaminD3

INTRODUCTION:

Thalassemia syndromes are caused by inherited mutations that decrease the synthesis of either alpha or beta globin chains of haemoglobin. Imbalance in globin chain synthesis results in anaemia, tissue hypoxia and red cell haemolysis. Individuals with β thalassemia major or homozygous type manifest with severe transfusion-dependent anaemia. Those with β thalassemia minor or heterogeneous genotype present with mild asymptomatic anaemia. The heterogeneous variant of moderate severity is called βthalassemia intermedia[1].

Thalassemia syndrome is endemic in Mediterranean basin, Middle East, tropical Africa, Indian subcontinent, and Asia. In India, itis the most common single-gene disorder. Every year one-tenth of the world's thalassemia population are born in India.

Recentdata indicate that about 7 % of the world's population is a carrier of a haemoglobin disorder[2]and that 300,000 - 500,000 children are born each year with the severe homozygous state of the disease worldwide. Every year approximately 100,000 are born with thalassemia in India. The carrier rate for thalassemia gene varies from 1-3% in southern India to 3-15% in Northern India[1].

According to WHO the average frequency of carrier state for thalassemia is 3.3% in India[3].

Thalassemia affects physical growth and delays maturation. Its management also imposes a huge economic burden on the families of the affected[1].Experiences from other endemic countries in Europe have shown that public education followed by screening and genetic counselling can substantially reduce the incidence of thalassemia[1].

Hospital-based registers give a good approximation of the disease pattern in the community when there is unavailability of formal population-based screening of haemoglobinopathies[1].

OBJECTIVE:

The present study was undertaken:

To evaluate the socio-demographic factors Growth parameters and analyse them with serum ferritin, average pretransfusion Hb, serum vitaminD3 in the transfusion dependent β-Thalassemia children between 2-18years of ages attending a Red Cross Transfusion centre located in district hospital, Eluru in West Godavari district of Andhra Pradesh.

METHODOLOGY:

This cross-sectional observational study was conducted during April to September of year 2019 in Red-cross recognised transfusion centre located in District Hospital in Eluru town with permission of the concerned authorities. Seventy seven transfusion dependent β-Thalassemia children of both sexes between the ages of 2 years to 18 years were the population under this study. Three ml of EDTA anticoagulated blood was drawn from all these cases with proper aseptic precautions[4].

INCLUSION CRITERIA:

Children between 2-18 years of age who are diagnosed to have thalassemia major based on HPLC and receiving regular transfusions[5].

EXCLUSION CRITERIA:

- Children <2years or >18years of age
- Children who are diagnosed as thalassemia minor or trait
- Children with congenital diseases/chronic illness and other haemoglobinopathies
- If the parents not willing to give consent

DATA COLLECTION AND ANALYSIS:
Detailed history was collected by using predetermined questionnaire, Demographical data like age, gender, age at time of diagnosis, Family history of consanguinity and carrier status are collected. Anthropometric measurements like height, weight, body mass index were taken and plotted on WHO Standard Growth charts and derived Z-scores are classified as 4 categories. Three ml of EDTA anticoagulated blood was drawn from all these children with proper aseptic conditions for the analysis of all the lab parameters.

From the collected data, means of the three investigations -Serum Ferritin, Vitamin D3 and Average pretransfusion Hb are estimated and grouped according to z-scores of Anthropometric parameters using MS Excel and SPSS 23 software.

RESULTS:
Age at diagnosis: Age at diagnosis being divided into 3 subgroups. The first sub group being 0-6 months in which 51 children affected with a highest percentage of 66.2% , The second sub group being 6month – 12 months with a involvement of 18 children (23.4%) and last sub group of> 12 months with 8 children (10.4%).

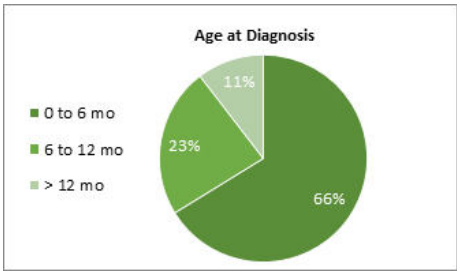


Fig 1: Age at diagnosis

Sex Distribution:
Males are being more affected n=48 (62.3%) compared to Females n=29 (37.7%).

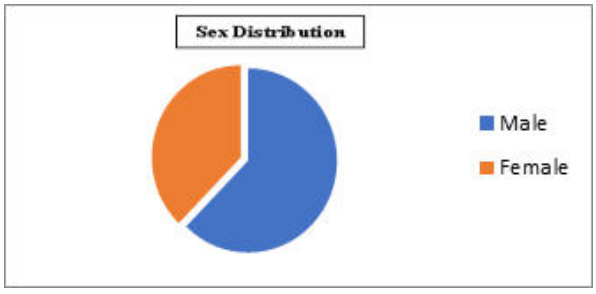


Fig: 2

Consanguinity:
In our study there is a very small difference in Consanguinity and non-consanguinity (1.2%).

Table: 1

Variables	Number	Percentage
Consanguinity		
• Yes	38	49.4%
• No	39	50.6%
Carrier Status		
• Yes	40	51.9%
• No	37	48.1%

Carrier status:
Among the 77 children with transfusion dependent β-Thalassemia with any one positive carrier in the family is being high n=40 (51.9%) compared to the No carrier in the family n=37 (48.1%).Among the Carriers status mother alone as a positive carrier contributing highest percentage of 42.9% followed by Father alone: 40.3% and both Father, mother: 33.8% last being sibling carrier of 23.4%.

Table.2: Pre transfusion haemoglobin levels:

	Sex	N	Mean	SD
Avg. Hb	Female	29	7.97	1.416
	Male	48	7.46	0.799

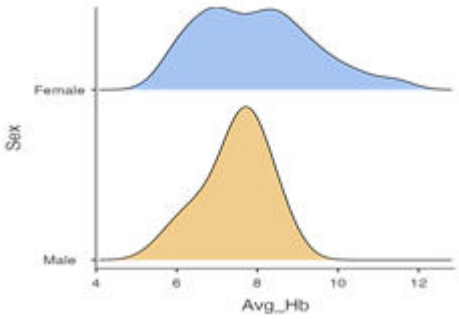
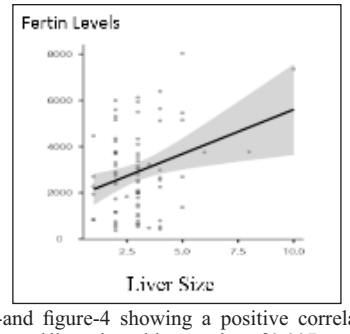


Fig: 3

Table.3:Correlation between Liver size and average Ferritin Levels

		Liver Size
Ferritin_Avg	Pearson's r	0.306
	p-value	**0.007**

Fig : 4



Here table 3-and figure-4 showing a positive correlation between average ferritin and liver size with a p-value of 0.007.

Table: 4

Z-scores	Frequency	Mean Serum Ferritin	Mean Vitamin D3	Mean Average Hb
Weight				
<-3	2	1711.2	22.5	7.2
-2 to -3	7	16,887	31.7	8.01
-2 to 0	54	2946.4	33.5	7.62
0 to +2	14	2901	30.12	7.65
Height				
<-3	14	2950	30.06	7.6
-2 to -3	13	2922	31.14	7.86
-2 to 0	38	2996	32.9	7.7
0 to +2	12	2630	35.33	7.4
BMI				
<-3	1	4337	22.5	7.2
-2 to -3	2	2523.5	31.7	6.2
-2 to 0	47	2838.6	33.5	7.6
0 to +2	27	3127.3	30.12	7.8

Weight: In our study it is being categorised into four subgroups by Z-scores, hetable here revealed that z-score of <-3(n=2) with a mean Serum Ferritin-1,711.2ng/ml, mean of vitaminD3: 22.5ng/ml and mean pretransfusion Hb: 7.2g/dl. This category being with lowest in all variables compared to the other sub groups, the other beingz-score of -2 to -3 (n=7) with mean serum ferritin:3080.14ng/ml and mean pre-transfusion Hb: 8.01g/dl, being highest compared to all sub groups and with mean vitaminD3: 31.7ng/ml.

In the third subgroup with the z - score of -2 to 0(n=54) is being highest in frequency and meanvitaminD3:33.5ng/ml compared to other sub groups with a mean serum ferritin: 2946.4ng/ml and mean pre-transfusionHb: 7.62g/dl.

The last subgroup being 0 to +2 (n=14) with serum ferritin: 2901ng/ml andvitaminD3 is 30.12ng/ml and mean average pre-transfusion Hb of 7.65g/dl.

Height: Height in our study being categorised into 4 sub-groups by z-scores.

The first subgroup with z-score <-3 (n=14) with mean of serum ferritin: 2950ng/with lowest mean value of vitaminD3:30.06ng/ml compared to other subgroups and mean pre-transfusion Hb: 7.6g/dl.

Second subgroup with z-score of -2 to -3 (n=13) with highest value of the mean pre-transfusion Hb: 7.86g/dl compared to other subgroups and mean serum ferritin: 2922ng/ml and mean Vitamin D3:31.14ng/ml.

The third sub group with Z-score -2 to 0 with highest frequency (n=38) and mean Z serum ferritin: 2996ng/ml with mean vitaminD3:32.9ng/ml and mean pre-transfusion Hb: 7.7g/dl.

The last subgroup being z-score of 0 to +2 with lowest of the values frequency n=12 and meanserum ferritin: 2630ng/m land mean pre-transfusion Hb: 7.4g/dl but with highest mean of vitamin D3:35 .33ng/ml.

BMI: BMI with z-scores of < -3 (n=1) is lowest in frequency and mean vitamin D3and with highest mean value of serum ferritin: 4337ng/ml and the mean pre-transfusion Hb: 7.2g/dl.

The second subgroup with z-score of -2 to -3 (n=2) with lowest mean serum ferritin: 2523.5ng/ml and mean pre-transfusion Hb: 6.2g/dl, mean vitaminD3:31.7ng/ml.

The third subgroup being z-score of -2 to 0 (n=47) with highest frequency and mean vitaminD3:33.5ng/ml compared to other subgroups with mean serum ferritin: 2838.6ng/ml and mean pre-transfusion Hb: 7.6g/dl.

The last subgroup being z-scores 0 to +2 (n=27) with highest mean pre-transfusionHb: 7.8g/dl and mean serum ferritin= 3127.3ng/ml,mean vitaminD3 levels 30.12ng/ml.

DISCUSSION:

The present study is a cross-sectional observational study to evaluate socio-demographic factors and growth patterns in transfusion dependent in β-Thalassemia and mean of investigations Vitamin D3,Serum Ferritin and average Hb are grouped according to Z-score of Anthropometric parameters in children regularly attending for blood transfusions at Red Cross transfusion centre Eluru. Thalassemia syndromes are caused by inherited mutations that decrease the synthesis of Haemoglobin. Imbalance in the globin chain synthesis results in hemolysis[1].Homozygous type manifest with severe transfusion dependent Anaemia. Blood transfusions can restore an acceptable amount of red blood cells, making the symptoms of anaemia disappear or decrease significantly. However, repeated transfusions children may develop complications related to Iron overload include growth retardation and failure or delay in sexual maturation. In our present study most of the children age at diagnosis found to be 0-6months (n=51) with a 66.2%. Males are being more affected n=48 (62.3%) compared to females. Similarly Simha chalamet.al, and many other studies revealed males are more affected[4].Consanguinity and positive carrier status being important factors for the occurrence of disorders. In our study positive carrier status is more related to disease compared to no carrier. Mother alone as a carrier contributes highest percentage for the occurrence of disease (42.9%). High serum Ferritin level may cause growth retardation in the study of Rathuret.al growth pattern in thalassemia children and their correlation with Serum Ferritin found correlation between Serum Ferritin and short stature and incidence of short stature which (p=0.001) which was thought to be due to Iron overload in Endocrine glands producing growth disorders[6]. Shalitinet.al., observed that short stature occurred when Serum Ferritin level were >3000ng/dl[6].Vogiatzet.al.,reported that 12% of that patients were Vitamin D deficient and 69.8% had insufficient levels[7].Jainet.al., reported 28% of Patients had height <5thcentile[7].

CONCLUSION:

In our present study socio-demographic factors such as males are affected more than females. Age at diagnosis was more in 0 to 6 months, children with carrier in the family were found to more than those without carrier in the family. The lab parameters like serum ferritin,vitaminD3, average pre-transfusion Hb were analysed for differentz-score categories of height, weight, BMI and they showed uniform distribution. Among the clinical features, we found statistically significant correlation between liver size and average ferritin levels. Growth retardation was noted in several children despite regular transfusions and chelation therapy. The causes may be multifactorial and hence these children must be assessed periodically for growth retardation using appropriate growth charts and treated accordingly as per guidelines of Thalassemia international federation.

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