Human Biology Review (ISSN 227 7 4424) 5 (3) 2016
©Human Biology Review Original scientific paper (Jana et al. pp. 349-360)
www.humanbiologyjournal.com Revised and Accepted on June 27, 2016

Correlation between nutritional status and clinical parameters among Thalassaemic patients – A study of West Bengal

A. Jana[1], A. Das Gupta[2], M. Bhattyacharyya[3], B.N. Sarkar[4]

Citation: Jana A, Das Gupta A, Bhatyachariyya M and Sarkar BN. 2016. Correlation between nutritional status and clinical parameters among Thalassaemic patients – A study of West Bengal. Human Biology Review, 5 (3), 349-360.

[1]**Arpita Jana, A**nthropological Survey of India, 27 Jawaharlal Nehru Road, Kolkata-700016, India. Email: **arpitaanthro2016@gmail.com**
[2]**Amrita Das Gupta**, Anthropological Survey of India, 27 Jawaharlal Nehru Road, Kolkata-700016, India. Email : **amritaanthro@gmail.com**
[3]**Maitreyee Bhattyacharyya**, Dept. of Haematology, Calcutta Medical College and Hospital, Kolkata, India. Email: **mbhattyacharyya@yahoo.co.in**
[4]**B.N. Sarkar**, Anthropological Survey of India, 27 Jawaharlal Nehru Road, Kolkata-700016, India. Email: **drbnsarkar@gmail.com**
Corresponding author: [1]Anthropological Survey of India, 27 Jawaharlal Nehru Road, Kolkata-700016, India. Email Id: arpitaanthro2016@gmail.com

ABSTRACT*: Thalassaemia is the most common monogenic, autosomal recessive hereditary disorder. The severe forms of thalassaemia are associated with chronic transfusion dependent haemolytic anaemia. Normal growth is impeded due to nutritional deficiency, chronic anaemia as well as iron overload. The aim of this study is to focus the nutritional health status of transfusion dependent thalassaemia patients. This is a cross-sectional analysis of the records of the patients registered at Day Care unit of a City Hospital, Kolkata, India. Clinical history of each patient is collected from registered book of the hospital and body weights and height of the patients are taken from day care unit before starting the transfusion. Laboratory parameters like Pretransfusion Haemoglobin (Hb) and Periodic Serum Ferritin are noted in respect of each patient. Z score for height, weight and Body Mass Index (BMI) is also taken into consideration using WHO reference. Statistical analysis was carried out using Microsoft excel and SPSS16 Software. Out of 117 Bengali speaking patients 84 were from different Hindu caste families and the rest 33 were from the Muslim community. The mean age of studied patients' population was 10.77 years (range 4 -20years). Major patients (81.1%) suffer high level (>1000ng/ml) of serum ferritin level due to not proper management of Pretransfusion haemoglobin and as well as not taken regular chelation. About two third (65.8%) of studied population are noted to be short stature, 18.8% are thin and 23.9% are very thin (BMI Z score <-3). as well as regular chelation therapy is the central aspects to improve their proper growth Only 3 children are overweight. Height Z scores is significantly co related with mean serum ferritin level. Management of the disease is very important to control the nutritional health status of thalassaemic children. Proper knowledge of iron free food, optimum transfusion as well as regular chelation therapy is the central aspects to improve their proper growth.*

Key Words*: Thalassaemia, serum ferritin, Z score, growth.*

INTRODUCTION:

Numerous disorders of the β globin chain of Haemoglobin molecule are responsible for various phonotypical diseases. Among them β thalassaemia is a subset of the heamoglobinopathies characterised by a hereditary anaemia with a wide phenotypic continuum that can have significant mortality and morbidity (Weatherall *et al.,* 2001a). In spite of that, thalassaemia is preventable by premarital counselling and prenatal diagnosis. The overall β thalassaemia carrier in India varies from 1% to 17% among different ethnic groups (Weatherall *et al.,* 2001b). Due to lack of proper documentation, precise data pertaining to occurrence and prevalence of the disease are unavailable. However, different studies statistically estimate that in India, around 80 to 90 percent of the 10,000 babies born each year with the disease die from it. Regular blood transfusion is the only remedy for thalassaemia patients. Iron overload is a key problem of transfusion dependent individuals and iron chelation therapy is the only preventive measures to control such iron overload. This chelation therapy is being practiced for the last two decades for the treatment of thalassaemia patients (Olivieri *et al.,*., 1997)**.** It should be started as soon as possible at least before reaching iron accumulation in a clinically significant stage; it may be presumed that the time has come to give a patient iron chelation therapy when he or she has received 10-20 times of red cell transfusion. Early initiation of Desferooxamine (DFO), a fundamental drug used widely as iron chelating therapy, before the age of 10 years, assures normal puberty in majority of patients (Bronspiegel-Weintrob *et al.,* 1990)**.** However, the initiation of DFO in young age may cause bone toxicity which may decrease growth (De Sanctis *et al***.,** 1994). Endocrine dysfunction is another problem which a thalassaemia patient has to face due excessive iron overload (Grundy *et al.,* 1994)**.**

Physical growth of a huge number of patients is severely affected with regular transfusion dependent thalassaemia. A study on some Saudi patients suffering from thalassaemia, aged 10-27 years, found short stature in 70 % of the male and 73% of the female (Najafipour *et al.,* 2008) and another study from China, reported short height in 29.7% of the patients (Li *et al.,* 2002)**.**

The most common endocrine abnormalities in thalassaemic children include hypogonadotropic hypogonadism, growth hormone deficiency and diabetes mellitus. Normal rates of prepubertal linear growth are observed in patients with regular

transfusion programs, but poor pubertal growth and impaired sexual maturation have been observed in well transfused patients (Kattamis *et al.,* 1970). Desferooxamine (DFO) has been employed in the treatment of beta thalassaemia but most of the patients do not have access due to their poor economic condition and as well as lack of awareness.

The purpose of the present study is to assess the physical growth of transfusion dependent thalassaemia patient.

MATERIAL AND METHODS:

The participants included in this cross sectional study are 117 (50 Female and 67 Male) transfusion dependent thalassaemia patients, taken regular blood transfusion from a thalassaemia day care unit at Nil Ratan Sarkar Medical College and Hospital, Kolkata, India. Ethical approval of the research project related to human subjects was obtained from the Institutional Ethical Committee of Anthropological Survey of India, Ministry of Culture, Government of India. The participated patients mainly belong to different district of South Bengal and are ethnic Bengali speakers. The age group of studied patients varies from 4 years to 20 years. Medical histories of all the patients are taken from the hospital record and other necessary information including sex, age, weight and height were also collected after obtain a written consent from the patients as well as parents of the patients. Anthropometric measurements were taken following the standard techniques of Lohman (Lohman *et al.,* 1988). Height and weight were recorded to the nearest 0.1 cm and 0.5 kg, respectively. The entire records of the registered patients were reviewed during the year 2011 to 2012. Information on the number of transfusion received, pre transfusion Hb levels, and Serum ferritin level measured in the previous 6-12 months were obtained from these records.

Most of the patients visited the day care unit every 3 to 4 weeks for blood transfusion. Serum ferritin level was recorded at that time. Doctors prescribe Deferiprone at a dosage of 75 mg/kg /day or Defrasirox (35-40mg/kg/day) when the ferritin level was >1000ng/ml. Both the drugs usually help in iron chelation. But most of the patient's families could not afford it due to their poor economic condition.

The following formula was used to calculate the Z score of an observed value of weight for age, height for age and LMS values were obtained from the World Health

Organization (WHO 2007) growth reference expanded tables for constructing national health chart.

Z score = $[(\text{observed value} \div M)^{L} - 1]/L*S$

This formula sometimes is called the LMS formula (WHO 2008) where

M = Median value of reference population

L = Power needed to transform the data in order to remove Skewness.

S = Co- efficient of variation.

Statistical analysis

All data were analyzed with SPSS (Statistical Package for social sciences, Version 16, SPSS) and Microsoft Excel. Data were presented as mean and standard deviation of mean (Mean ± SD). Statistical significance was assumed at the 1% and 5% level.

RESULTS:

In the present study, 117 Bengali speaking children, aged 4-20 years coming from different Hindu Caste families as well as Muslim families of different district of South Bengal were participated. They took regular transfusion at the Day Care Unit of the city hospital. Out of 117 participants, 84 were from Hindu Bengali families and 33 from Muslim Families. Among Bengali Hindu Caste families, 33.4% participants belonged to Poundrakhatriya. Graphical presentation of Community wise distribution of studied participant is shown in figure 1and Table 1 exhibit the descriptive statistics of the clinical characteristics of the participants. Mean age of studied participant was 10.77 years and the number of adolescent (>10years) participants was more than infants (<10 years). Out of 117 participants, 67 were boys (57.3%) and 50 were girls (42.7%).

Pre-transfusion Hb level was not well maintained, with mean Hb level 6.51±1.03, (range 3.1 g/dl to 9.6 g/dl) whereas 78 (66.7%) had pre-transfusion Hb level below 7.0 g/dl.(Table: 1). Only one patient, who was 11 year old, was in the worst condition and his Hb level was 3.1 g/dl . Mean serum ferritin level was 1180.71±263.45 ng/ml among the studied patients group. The minimum value (288.70 ng/ml) was observed in a new patient who was only 4 years old and the maximum value (1836.50 ng/ml) was observed in a 15 years old boy. The difference between the mean ferritin levels of boy

and girl patients was not statistically significant. The majority of studied participants (105 of 117 or 89.7%) had not taken the regular chelation therapy due to their poor economic condition and 76% of studied participant had splenomegaly and the percentage of splenectomise patient 20.51% (table 1). Splenectomise is the process for better treatment of thalassaemia patient.

The mean Z score of height for age HAZ was [stunted (short stature)] -2.61±1.50 and only 16.23% of the patients were normal stature. The mean Z score for weight for age WAZ was (underweight) -3.45 ± 1.89 and only 24.7% patients were normal weight (WAZ >-2). Although, 50 patients (42.7%) were undernourished (thinness is 18.8% and severe thinness 23.9%; BMI for age Z scores < -2 and < -3, respectively). Only 3 patients had overweight and they are below 10 years of age group.

Correlation between age and WAZ, HAZ, BMIZ score and mean ferritin level were calculated and presented in table 2. The result shows that the Serum ferritin level of the male participant group is negatively correlated with HAZ and WAZ. Entire studied population also shows the same result. We can conclude that when the amount of Serum ferritin level increases, the HAZ and WAZ decrease. But there is a very weak relationship between ferritin level and HAZ, WAZ. Whereas, Female group shows the positive correlation with HAZ and WAZ but it is not strongly correlated.

Regression analysis between height Z score and mean ferritin levels was significant (regression coefficient -1.857, standard error 0.625, t = -2.972, *P = 0.004*). Mean Serum ferritin level was higher (1215.97 ± 257.53 vs. 1120.06 ± 265.45, P = 0.05) in the adolescence (>10years) group than the children (<10 years) group. Only 20 patients had normal height where as rest of the adolescent patients (54) had short stature (Table 3).

Height Z score was further analysed at different ages according to ferritin level (Table 4). The result exhibit that age wise height Z score was higher among children with the serum ferritin >1000 ng/ml than those children had serum ferritin below 1000 ng/ml. Among patients with high ferritin level, few had normal height and they also taken regular chelation therapy in spite of their iron overload being much higher. So, individual study as well as observation is needed to scrutinize proper growth of thalassaemic children.

In this present study, the number of adolescence patient (>10years) was higher than children (<10years) due to the presence of disease and as well as complication of disease. According to Table 3 the adolescence group patients were in worse situation than the children group. One interesting observation was that only 3 children had overweight and they were below 5 year age and they was newly registered patient at Day Care Unit.

DISCUSSION:

BMI is one of the important methods to assess underweight and normal health. Patients with thalassaemia major are exposed to many growth abnormalities due to continuous blood transfusion and excessive iron overload stored in many organ systems. So, it is important to reduce this impairment by chelating the excess iron and also monitoring the side effects. Present participants received regular transfusion, out of which only 13 children had taken regular iron chelation therapy. Most of them, though, could not receive this medical procedure due to their poor economic condition. This excess stored iron is increased serum ferritin level but many of the patients were unable to test the level at particular time duration. This is the main cause for the complication of thalassaemia.

About 65.8% of the studied patients were short stature and 42.73% of the participants were thin or severely thin (Table 3). Height for age (HAZ) was related to mean ferritin levels. The mean of serum ferritin level depend on so many factors, including age at presentation, age at 1st date of regular transfusion, and age at starting iron chelation drug. In the present study, the transfusion dependent patients are consistent with serum ferritin levels of more than 1200ng/ml observed in adolescent group. Only 13 patients had below 1000ng/ml of serum ferritin level because they maintain proper chelation therapy. So, iron chelation therapy is an important factor to reduce excess iron which causes several complications of thalassaemic children (Eleftherion 2003).

Regression analysis between height Z scores and mean ferritin levels was significant (regression co-efficient -1.857, standard error 0.625, t = -2.972, P = 0.004) [Table 5]. It is noted that excess iron is responsible for short stature. This fact is better shown by the regression fit analysis in figure 2.

This type of approximation can be better predicted by a longitudinal study, so many studies have noted similar type of findings. One study from Malaysia revealed that the mean ferritin level of thalassaemic children with a height under the 3rd percentile was higher compared to those with a height over the 3rd percentile (Hamidah *et al.,* 2008). Another study from India found that mean ferritin level was significantly higher in patient with short stature than in the patients with normal height (Pemde *et al., 2011*).

Previous study reported from Iran indicated that 70% of boys and 73% of girls over 10 years of age with transfusion dependent thalassaemia had short stature which is constant with the present study .This study also noted that short stature becomes more prominent during adolescence.

Iron chelation is an important therapy to reduce excess iron. The adult height of patients depends on the efficacy of iron chelation, especially during prepubertal age where regular blood transfusion beside with maintaining Hb level and simultaneously regular chelation therapy is needed for better treatment of thalassaemia patient because high serum ferritin level can weigh down the physical growth of patient, especially in second decade of life. More efficient iron chelating drugs are needed to reduce the complication related to deposition of iron. But the present studied patients are incapable to accept any kind of drug or therapy due to their poor economic condition and as well as lack of proper awareness.

CONFLICT OF INTERESTS

The authors declare no conflict of interest for the present research outcome.

ACKNOWLEDGMENTS

We would like to thank the members of the study populations for their cooperation during data collection. We wish to express our deep gratitude to the Director, Anthropological Survey of India, for his kind permission to initiate the work and also for providing financial support.

REFERENCES:

Bronspiegel-Weintrob N, Olivieri NF, Tyler B, Andrews DF, Freedman MH, Holland FJ.1990.Effect of age at the start of iron chelation therapy on gonadal function in beta-thalassemia major.*N Engl J Med*. Sep **13**; 323(11):713-9.

De Sanctis V, Katz M, Vullo C, Bagni B, Ughi M, Wonke B. 1994.Effect of different treatment regimes on linear growth and final height in beta-thalassaemia major. *Clin Endocrinol (Oxf).* Jun; **40**(6):791-8.

Eleftherion A.2003 About thalassaemia, *Thalassaemia International Federation Publication* (4), Cyprus; 69.

Grundy RG, Woods KA, Savage MO, Evans JP.1994. Relationship of Endocrinopathy to ironchelation status in young patients with thalassaemia major. *Arch Dis Child*. Aug; **71** (2) :128-32.

Hamidah A, Arini MI, Zarina AL, Zulkifli SZ, Jamal R.2008. Growth velocity in transfusion dependent prepubertal thalassaemia patients: results from a thalassaemia center in Malaysia. *Southeast Asian J Trop Med Public Health*. **39**: 900-905.

Pemde HK, Chandra J, Gupta D, Singh V, Sharma R, Dutta AK. 2011. Physical growth in children with transfusion dependent thalassaemia, *Pedriatic Health medicine and therapeutics:* **2** 13-19.

Kattamis C, Touliatas N, Haidas S, Matsaniotis N.1970. Growth of children with thalassaemia. Effect of different Transfusional regimens. *Arch Dis Child* . **45**, 502.

Li CK, Luk CW, Ling SC, et al.2002. Morbidity and mortality patterns ofthalassemia major patients in Hong Kong: retrospective study. *Hong Kong Med J*. **8**:255–260.

Lohman TG, Roche AF and Martorell R. 1988. *Anthropometric Standardization Reference manual*.Human. Kinetics Books, Chicago.

Najafipour F, Aliasgarzadeh A, Aghamohamedzadeh N, et al.2008. A cross-sectional study of metabolic and endocrine complications in beta thalassemia major. *Ann Saudi Med*. **28**:361–366.

Olivieri NF, Brittenham GM.1997. Iron chelating therapy and the treatment of thalassaemia. *Blood.* Feb 1:**89** (3): 739-61.

Training course on Child Growth Assesment WHO Child Growth Standards. Interpreting growth standards.2008. *WHO* :**48**.

Weatherall DJ, Clegg JB.2001a. *The Thalassaemia Syndromes*. **4Th** ed. Oxford, England:
Black well science.

Weatherall DJ, Clegg JB.2001b. Inherited haemoglobin disorders: an increasing global health problem. *Bull World Health Organisation*.**79**: 704-712.

WHO Growth Reference 2007. http:// www. Who.int/growthref/en/. Accessed on Mar 6, 2010.

Table 1: Clinical parameters of participants with transfusion dependent thalassaemia

Parameters	Number (%)
Total number of participants	117(100%)
Male children	67(57.26%)
Female children	50 (42.73%)
Mean age ±SD(years)	10.77 ± 3.46
Mean weight Z Score	-3.45 ± 1.89
Mean Height Z Score	-2.61 ± 1.50
Number of patients with weight Z score <-2	88(75.21%)
Number of patients with height Z score <-2	77(65.81%)
Mean BMI Z score	-2.20 ± 2.91
Number of patients with BMI Z score <-2	50(42.73%)
Hepatomegaly (liver size>1 cm)	94(80.34%)
Splenomegaly (Spleen size >1cm)	89(76%)
Splenectomised	24(20.51%)
Mean Serum Ferritin level (ng/ml)	1180.71 ± 263.45
Mean Hb level(g/dL)	6.51 ± 1.03
No. of patients do not taken chelation	105(89.7%)

Table 2: Pearson Correlations between anthropometric variables and Serum ferritin level

			HAZ	WtZ	BMIZ	Height	Weight	BMI
SERUM FERRITIN	MALE (N=67	Pearson Correlation	-0.196	-0.117	0.071	0.2	0.217	0.144
		Sig. (2-tailed)	0.111	0.346	0.566	0.105	0.077	0.246
	FEMALE (N=50)	Pearson Correlation	0.011	0.151	0.156	-0.095	-0.084	0.068
		Sig. (2-tailed)	0.938	0.295	0.278	0.512	0.564	0.638
	TOTAL (N=117)	Pearson Correlation	-0.115	-0.014	0.089	0.049	0.072	0.117
		Sig. (2-tailed)	0.216	0.882	0.342	0.597	0.442	0.208

Table 3: Distribution of growth pattern of children and adolescence group

Category (N=117)	SF	STUNTED (HAZ <-2SD)	UNDERWEIGHT (WAZ <-2SD)	THINNESS (BMIZ<-2SD)	OVERWEIGHT (BMIZ >+1SD)
Children (<10years) N=43	1120.06 ± 265.45	23(55.8%)	25(58.1%)	16(37.2%)	3(6.97%)
Adolescence (>10years) N=74	1215.97 ± 257.53	54(72.9%)	63(85.1%)	36(48.6%)	0(0%)
		77(65.8%)	88(75.2%)	52(44.5%)	3(2.56%)

Table 4: Age wise Height Z score and serum ferritin levels in children with transfusion dependent thalassaemia

Serum ferritin (ng/ml)	< 5 years		5-10 years		10-15 years		>15 years		All	
	No.	Height Z score	No.	Height Z score	No	Height Z score	No	Height Z score	No	Height Z score
<1000 ng/dl	1	0.22	8	-2.62 ± 1.48	9	-2.99 ± 0.96	4	-3.44 ± 1.00	22	-2.34 ± 1.80
>1000 ng/dl	1	-4.18	49	-2.72 ± 1.36	37	-3.10 ± 1.20	8	-4.03 ± 1.13	95	-2.67 ± 1.42

Table 5: Regression Analysis between HAZ and Serum Ferritin level

Coefficients[a]						
Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	-1.857	.625		-2.972	.004
	SF	.000	.001	-.115	-1.244	.216
a. Dependent Variable: HAZ						

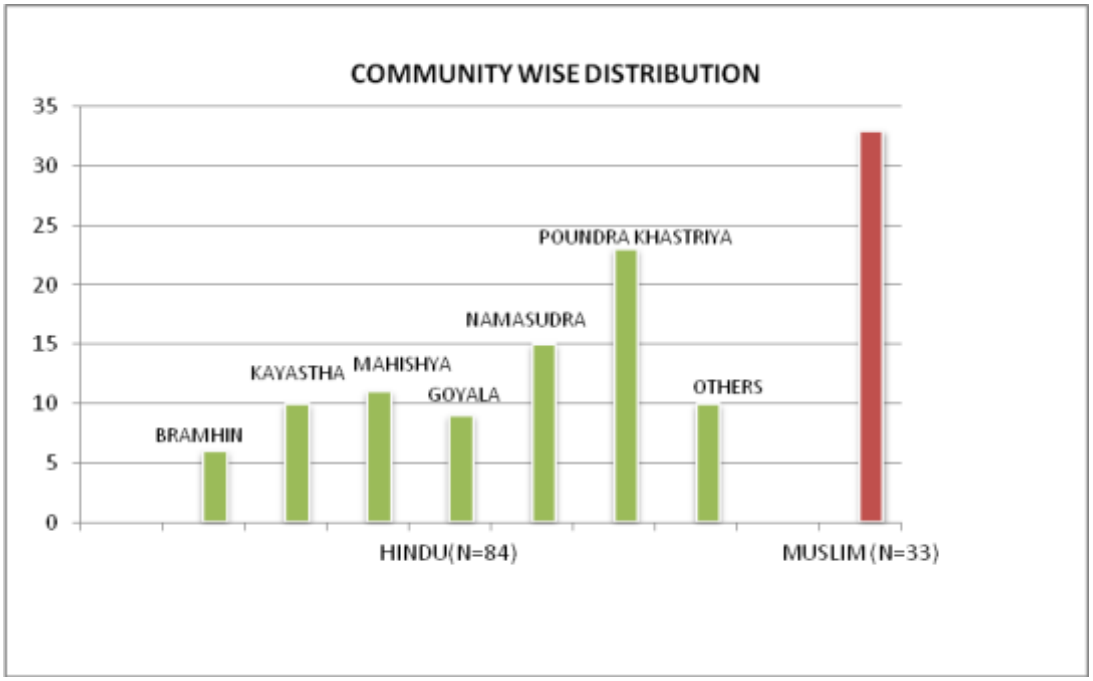

Figure 1: Community wise distribution of studied participants

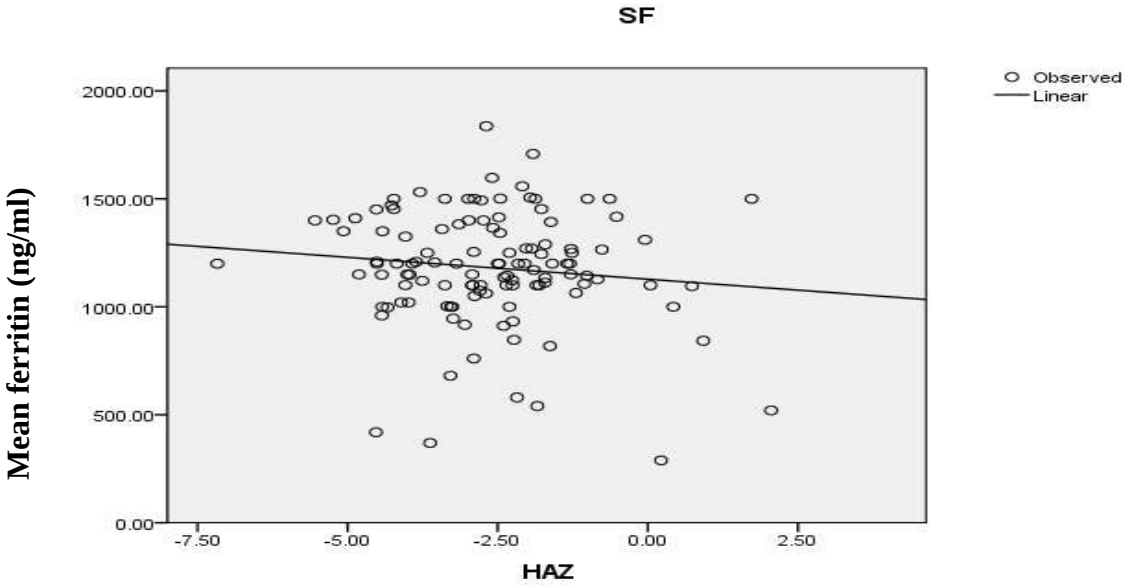

Figure 2: Regression fit between mean serum ferritin levels (ng/ml) and height z- scores in children with transfusion dependent Thalassaemia