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Original Research Paper

Hematology

ASSESSMENT OF ENDOCRINE DYSFUNCTION AND IRON OVERLOAD IN MULTI-TRANSFUSED BANGLADESHI THALASSEMIA PATIENTS

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ABSTRACT

In transfusion dependant Thalassemia patients under transfusion, and multiple transfusion along with inadequate chelation therapy leading to iron overload may cause endocrine complications. The aims of this study are to assays the endocrine dysfunctions and their correlation with iron overload. This retrospective study assays multi-transfused thalassemic children in Dhaka Shishu(Children) Hospital Thalassemia Centre of Dhaka Shishu(Children) Hospital. Among 135 patients, age range was 12-18 years and mean was 14.6 ± 2.50 years, 71(53%) were boys and 64(47%) were girls. Mean serum FSH was 1.37 ± 1.05 mIU/ml, normal in 21(33 %) and low in 43(67%) girls. Mean level of LH was 1.67 ± 2.05 mIU/ml, normal in 28(44%) and low in 36(56%) girls. Mean testosterone level was 16.30 ± 1.35 ng/dl, normal in 10(14%) and low in 61(86%) boys. Mean serum TSH was 3.37 ± 1.05 mIU/ml, normal in 103(7 6%) and high in 32(24 %) study population. Mean serum PTH was 58.63 ±7.47 pg/ml, normal in 105(77.2%), low in 13(9.7%) and high in 17(12.5 %) study population. Correlation between different hormonal imbalances with serum ferritin level was not found. The high prevalence of endocrine dysfunctions in this study justifies the need for regular follow-up of multi-transfused thalassemic children for early detection and appropriate treatment of endocrine dysfunctions.

KEYWORDS : Thalassemics, iron overload and endocrine dysfunction.

INTRODUCTION

Thalassemia is one of the most common hereditary diseases worldwide. It is an important health problem, causing much morbidity, early mortality and a lot of financial and emotional misery for a family[1].

Thalassemia is an important health problem in Bangladesh. Dhaka Shishu(Children) Hospital Thalassemia Center(DSHTC) has been diagnosed 901 β-thalassemia major and 2407 Hb E- β thalassemia in the last decade(According to the data of DSHTC). Daily 20-40 thalassemia patients are getting integrated management including blood transfusion in Dhaka Shishu(Children) Hospital Thalassemia Center(DSHTC) daily. These thalassemia patients come from all over the country.

Blood transfusion is essential for survival of thalassemic children while eventually leading to iron overload, resulting in various endocrine dysfunctions 2,3,4,5 Several authors have been studied over polytransfused and untransfused thalssemia patients with the findings of high incidence growth disturbances and endocrine dysfunction 6,7. Recently various authors have reported high incidences of growth retardation, delayed puberty and endocrine dysfunctions in polytransfused thalassemic patients 8,9,10.

In Bangladesh, more than 10,00 cases of thalassemia are born every year according to conservative data of WHO, yet no published data is available on the growth, puberty and endocrine status of these children.

This study was conducted to assess the growth, puberty and endocrine dysfunction and iron overload in multi-transfused Bangladeshi thalassemia patients.

OBJECTIVE

To assess the endocrine dysfunction and iron overload in multi-transfused Bangladeshi thalassemia patients.

MATERIALS AND METHODS

Study design

Cross sectional study.

Study place

Dhaka Shishu (Children) Hospital Thalassemia Center, Dhaka Shishu (Children) Hospital. Dhaka, Bangladesh.

Study period

1st January, 2016 to 31st May 2017.

Sample size

135 (64 females and 71 males).

Inclusion criteria

Hemoglobin E- β Thalassemia & β Thalassemia Major patients.
Age 12-18 years.
Registered in Dhaka Shishu(Children) Hospital Thalassemia Center.
Multitransfused.

Exclusion criteria

Age below 12 and above 18 years.
Patients with other chronic illness.

Procedure

Biochemical investigations like Serum ferritin, testosterone, FSH, LH, estradiol, thyroid hormones and PTH was estimated by Chemiluminescence methods.

Statistical analysis

Data were analyzed using SPSS (version 16.0).

Numerical data were represented as mean ± SD and mean comparison were done by unpaired t test.

Proportions were compared using the *Chi-square test.*

Confidence intervals were set at 95 and p value <0.05 was taken as significant.

Patient's characteristics

Male : 71 (53%)
Female : 64 (47%)
Mean age: 14.9 ± 2.5 yrs

Iron Chelating agents used:

- On Deferipon : 65 (48%)
- On Desferrioxamine:20 (15%)
- On both : 16 (12%)
- On Deferasirox: 28 (21%)
- On none : 06 (04%)

Transfusion history:

- Well transfusion : 44 (32.6%)
- Under transfusion: 91 (67.4%}

Mean blood transfusion requirement was 190 ± 14 ml/kg/yr, with a range of 155 to 224 ml/kg/yr

Twenty four patients of 135 (17.8%) underwent splenectomy.

RESULTS

In this study of total 135 patients, the age range was 12-18 years and mean age of the patients was 14.6 ± 2.50 years and 72(53%) were boys and 63(47%) were girls (Table-I).

Table-I: Age and sex distribution of studied subjects (n=135).

Variable	Mean ± SD/frequency	Range
Age	14.6 ± 2.5 years	12-18 years
Sex	Boys	Girls
	72(53%)	63(47%)

Among the total 135 cases 44 (32.6%) were well transfused and 91(67.4%) were under transfused.

Regarding anthropometric measurement of 135 studied subjects, the mean weight was 32.25 kg ± 8.45 kg, the mean height of was 136.22 cm ± 11.57cm. (Table-II).

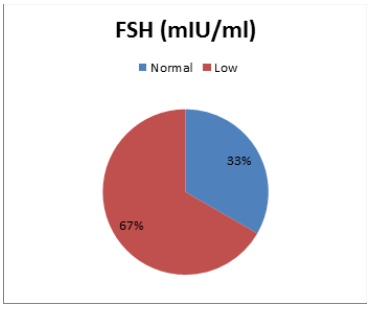
Table-II: Anthropometry of studied subjects (n=135).

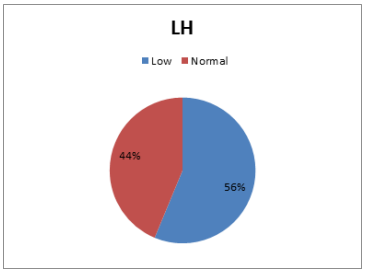
Parameter	Mean ± SD/frequency
Standing height	136.22 cm ± 11.57 cm
Weight	32.25 kg ± 8.45 kg

The mean serum ferritin level of all 135 cases was 4160 ± 2240 ng/ml (range 764-9273 ng/ml).

Regarding FSH in our study, the mean serum FSH was 1.37 ± 1.05 mIU/ml. FSH level was normal in 21(33 %) and low in 43(67%) girls. As regard LH level, the mean level of it was 1.67 ± 2.05 mIU/ml, while the level was normal in 28(44%) and low in 36(56%) study girls (Figure-I).

Figure I: FSH & LH levels in studied population (Girls) (n=64)





As regard relation between serum ferritin and hormonal (FSH) levels in our studied populations, 43(67%) girls had low FSH with mean serum ferritin level of 3790 ng/ml and 21(32.8%) girls had normal FSH with mean serum ferritin level of 3170 ng/ml and. Serum ferritin in relation to FSH level were statistically insignificant(P=0.49)(Table-III).

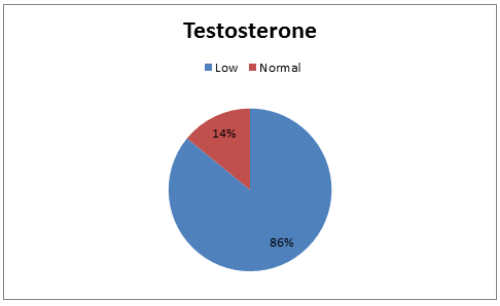
Regarding relation between serum ferritin and hormonal (LH) level in girls, 28(44%) had normal LH with mean serum ferritin level of 3065 ng/ml and 36(56%) had low LH with mean serum ferritin level of 3647 ng/ml. Serum ferritin in relation to LH level were statistically insignificant(P=0.53)(Table-III).

Table-III: Serum ferritin levels in relation to hormonal dysfunction (Girls) (n=64)

Hormones	Levels	Noof cases	%of cases	Meanserum ferritinng/ml	Pvalue	Significance
FSH (mIU/ml)	Normal Low	21 43	33 67	3170 3790	0.49	NS
LH (mIU/ml)	Normal Low	39 25	61 39	3065 3647	0.53	NS

Regarding testosterone level in study boys, the mean level was 16.30 ± 1.35 ng/dl, 10(14%) had normal and 61(86%) had low serum testosterone level (Figure-II).

Figure-II: Testosterone level in studied population (Boys) (n=71)



About relation between serum ferritin and hormonal level in boys, 10(14%) had normal testosterone with mean serum ferritin level of 3105 ng/ml and 61(86 %) had low testosterone with mean serum ferritin level of 4015 ng/ml. Serum ferritin in relation to testosterone level were statistically insignificant(P=0.58) (Table-IV).

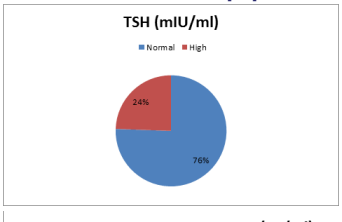
Table-IV: Serum ferritin levels in relation to hormonal dysfunction (Boys)(n=71)

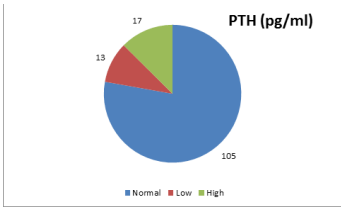
Hormones	Levels	No of cases	% of cases	Mean serum ferritin ng/ml	P value	Significance
Free testosterone (pg/ml)	Normal Low	10 61	14 86	3105 4015	0.58	NS

Regarding TSH in our study, the mean serum TSH was 3.37 ± 1.05 mIU/ml. TSH level was normal in 103(7 6%) and high in 32(24 %) study population (Figure-III).

As regard PTH level, the mean level of it was58.63 ±7.47 pg/ml, while the level was normal in 105(77.8%), low in 13(9.7%) and high in 17(12.5 %) study population (Figure-III).

Figure-III: TSH & PTH level in studied population (Boys) (n=135)





The level of TSH and PTH in relation to serum ferritin was insignificant (Table-V).

Table-V: Serum ferritin levels in relation to hormonal dysfunction (Boys & Girls) (n=135).

Hormones	Levels	Noof cases	%of cases	Meanserum ferritinng/ml	Pvalue	Significance
TSH (mIU/ml)	Normal High	103 32	76 24	3105 3850	0.47	NS
PTH (pg/ml)	Normal Low High	105 13 17	77.2 9.7 12.5	3249.0 4258.0 4467.0	0.45	NS

DISCUSSION

In this study, majority of the study cases (67.4%) were under transfused might be due to poor socioeconomic background and illiteracy. Hypogonadism is the most frequent endocrine complication in these patients which is also responsible for growth retardation in adolescence. Hypogonadotrophic hypogonadism is due to damage from iron deposition in the hypothalamus and pituitary gland but may occasionally be due to primary gonadal failure. Regarding endocrine status in this study, FSH levels were low in 67%, LH levels were low in 67% 10,11,12,13), but higher than the other study 6,14 Free testosterone levels were low in 78 % boys which are similar to the studies done abroad 6, 11, 14.

Subclinical hypothyroidism was present in 24% study population which is close to some other studies 6, but slightly higher than the study done by Agarwal MB et al 15 who reported subclinical hypothyroidism in 6.9% thalassemic children and overt hypothyroidism was present only in 2.3% cases like other few studies 16. Overt hypothyroidism found in under treated patients.

In the present study, 13 (9.7%) children had low PTH levels. The incidence of hypoparathyrodism is relatively common which varies from 3.6% to 22.5% in various other studies 17,18 and this study also showed that 17 (12.5%) children had high PTH level. Whether high PTH level is secondary due to Vitamin D deficiency or not-could not be determined as Vitamin D estimation was not included in this study. The postulated underlying causes of hypogonadism and delayed puberty are pituitary damage due to iron overload as well as chronic anemia in case of under transfusion.

CONCLUSION

This study supports the fact that the thalassemic children are growth retarded and have multiple endocrine dysfunctions which usually begin early in life along with under transfusion and iron overload.

RECOMMENDATION

Optimum blood transfusion, control of iron overload, and regular endocrine evaluation for early detection and treatment of associated complications are mandatory for their normal growth and life expectancy.

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