ORIGINAL ARTICLE

Correlation between Serum TSH and Serum Ferritin in patients of Beta Thalassemia Major

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ABSTRACT

Background: Beta Thalassemia is a hereditary disorder which is characterized by deficiency in the synthesis of beta-globin chains of Hemoglobin. β thalassemia is caused by mutations in the HBB gene on chromosome 11 and is inherited in an autosomal recessive pattern. This mutation causes the inability to synthesize new Beta chains resulting in overall decrease in the production of Hemoglobin A. This decrease leads to the development of microcytic anemia which can be very severe and usually requiring long term transfusions for the patient to survive.
Aim: To determine correlation between mean serum Ferritin levels and mean serum TSH levels of patients of β thalassemia major.
Study design: Cross sectional study
Settings: Department of pediatrics, Sahiwal Medical College, Sahiwal, from April, 2016 to October, 2016.
Results: Mean age of the patients was 8.73±2.569 years and mean duration of blood transfusion was 7.88±2.622 years, mean serum TSH was 3.8085±2.281 µIU/ml, mean serum ferritin was 3087.64±1.625ng/dl. Negative correlation between serum TSH and serum ferritin level was noted which was statistically insignificant (r=-0.014, P= 0.911).
Conclusion: Results of this study revealed that there is negative correlation between serum TSH and serum ferritin levels which was statistically insignificant. Results of this study also showed insignificant difference between mean serum TSH and mean serum ferritin levels of male and female patients was observed.
Keywords: Iron overload, β thalassemia major, Serum ferritin level, Correlation, TSH

INTRODUCTION

Beta Thalassemia is a hereditary disorder which is characterized by deficiency in the synthesis of beta-globin chains of Hemoglobin. β thalassemia is caused by mutations in the HBB gene on chromosome 11 and is inherited in an autosomal recessive pattern.[1] This mutation causes the inability to synthesize new Beta chains resulting in overall decrease in the production of Hemoglobin A. This decrease leads to the development of microcytic anemia which can be very severe and usually requiring long term transfusions for the patient to survive. These transfusions become a part of the disease as they can cause iron overload which in itself causes a lot of problems for the patients and chelation therapy is added to counteract the effects of this overload[2].

In β thalassemia major the mutated gene exists on both alleles. Other than anemia the patients are also predisposed to several complications. The excessive iron deposition affects the structure and function of the thyroid gland, this ultimately leads to hypothyroidism which is usually subclinical but can also manifest clinical symptoms[2]. It has been reported that these endocrinopathies occur in the second decade of life[3].

The frequency of hypothyroidism associated with β thalassemia major and its relation with iron overload has been a topic of controversy in the recent years, with some studies reporting that there is a definite relation between iron overload and hypothyroidism and other studies showing that there is no relation between the two whatsoever citing other causes for the reported hypothyroidism[4,5]. Garadah TS et al. in their study reported that higher serum TSH levels of the patients of β thalassemia major correlated positively with the levels of serum Ferritin (r=0.34, p=0.014) implying the link between the two[6]. Some studies conducted in the south Asian region demonstrate that prevalence of hypothyroidism in β thalassemia major varies according to the region, quality of management and treatment protocols, thus questioning the link between hypothyroidism and iron overload[7].

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As serum ferritin level raises in blood transfusion dependent Beta Thalassemia Major Patients and causing Endocrinopathies. A study is plan to determine the correlation between serum ferritin levels and serum TSH levels. The result of this study will guide us in the management of elevated serum TSH level in blood transfusion dependent Beta Thalassemia Major Patients if correlation found.

MATERIAL AND METHODS

This cross sectional was conducted at Department of Pediatrics, Sahiwal Medical College, Sahiwal. Total 66 patients of β thalassemia major were selected from April, 2016 to October, 2016.

Inclusion Criteria

1. Patients with β thalassemia major as per operational definition.
2. Patients on blood transfusion from last 5 years.
3. Age between 6 to 15 years.
4. Both male and female.
5. Patients taking 1-3 transfusions/month.

Exclusion Criteria

1. Patients undergoing bone marrow transplant
2. Previous history of any chemotherapy or radiotherapy.
3. Any history of goiter.
4. Any history of thyroxine intake.
5. H/O drug or alcohol abuse.
6. Patients with severe hepatic, renal or CVS dysfunction.
7. Any history of malignancy.

OPERATIONAL DEFINITIONS

β thalassemia major: Patient was labelled as patient of β thalassemia major when Hb<7gm/dl, microcytichyochromic anemia on peripheral blood picture and have >70% HbF on hemoglobin electorpholysis with hepatosplenomegaly (on clinical basis).

Mean serum ferritin level: It was measured in ng/dl.

Mean TSH level: It was measured in µIU/ml.

Data Collection Procedure: After permission from the concerned authorities and ethical committee and after taking informed consent from the attendants of patients, total of 66 patients with diagnosis of β thalassemia major were selected. The detailed history was taken. Blood samples were drawn from the patients before they undergo their current scheduled transfusion. Mean serum Ferritin and mean serum TSH levels were determined by chemiluminescence method on hormone analyzer Cobas E 411 by Roche in the department of Chemical Pathology. All patients were given same standard treatment. All the data was recorded on the specially designed prorforma.

Data analysis: Data was analyzed using SPSS version 22. Quantitative data like age, duration of blood transfusion, TSH, Ferritin levels and qualitative data like gender was analyzed. Mean and standard deviation was calculated for quantitative data like age and duration of blood transfusion. Frequency and percentages were calculated for analysis of qualitative data like gender. Pearson correlation coefficient was calculated for mean serum TSH and mean serum Ferritin levels. Effect Modifiers like age, duration of blood transfusion and gender were controlled by Stratification. Post Stratification T test was applied. P value ≤ 0.05 was considered as significant.

RESULTS

Mean age of the patients was 8.73±2.569 years and mean duration of blood transfusion was 7.88±2.622 years, mean serum TSH was 3.8085±2.281 µIU/ml, mean serum ferritin was 3087.64±1.625ng/dl.

Table 1 showing relation of serum TSH level with serum ferritin. The Pearson correlation test showed that the level of serum TSH decreased with increasing serum ferritin levels. This negative correlation was statistically insignificant (r=-0.014, P=0.911).

Mean serum TSH in male and female patients was 3.820±2.219 µIU/ml and 3.787±2.442 µIU/ml respectively. Comparison of mean serum TSH between male and female patients was done and insignificant (P=0.956) difference between mean TSH of male and female patients was noted. Mean serum ferritin levelin male and female patients was 3296.44 ±1752.368ng/dl and 2697.26±1301.453ng/dl respectively. Comparison of mean serum ferritin levelbetween male and female patients was done and insignificant (P=0.155) difference between serum ferritin levelof male and female patients was noted (Table 2).

Patients were divided into two age group, age group 6-10 years and age group 11-15 years. Mean serum TSH in age group 6-10 years was 3.688±2.151 µIU/ml and in age group 11-15 years was 4.186±2.690 µIU/ml. But the difference between mean TSH of both age groups was statistically insignificant with p value 0.451. Patients were divided into two age group, age group 6-10 years and age group 11-15 years. Mean serum ferritin levelin age group 6-10 years was 3005.90±1587.091ng/dl and in age group 11-15 years was 3343.06±1766.621ng/dl. But the difference between serum ferritin levelof both age groups was statistically insignificant with p value 0.474 (Table 3).

Division of patients according to duration of blood transfusion was done and two groups were

made 5-10 year group and 11-15 years group. Mean TSH in 5-10 year group was 3.676±2.116 µIU/ml in 11-15 years group mean TSH was 4.350±2.897 µIU/ml. insignificant (P=0.343) difference between the mean TSH of both group was noted. Division of patients according to duration of blood transfusion was done and two groups were made 5-10 year group and 11-15 years group. Mean serum ferritin level in 5-10 year group was 3089.09±1587.259 ng/dl in 11-15 years group mean serum ferritin levelwas 3081.69 ± 1839.551 ng/dl. Insignificant (P=0.988) difference between the mean serum ferritin level of both group was noted. (Table 4)

Table 1: Correlation of serum TSH with serum ferritin

	TSH (µIU/ml**)**	
	Pearson correlation(r)	P-value
serum ferritin (ng/dl)	-0.014	0.911

Table 2: Comparison of mean serum TSH and mean serum ferritin level between male and female patients

Gender	**n**	**Mean**	**Std. Deviation**	**P value**
Mean serumTSH				
Male	43	3.820	2.219	0.956
Female	23	3.787	2.442	
Mean serum ferritin				
	43	3296.44	1752.368	0.155
Female	23	2697.26	1301.453	

Table 3: Comparison of mean TSH between different age groups

Age group	**n**	**Mean**	**Std. Deviation**	**P value**
Mean TSH				
6-10	50	3.688	2.151	0.451
11-15	16	4.186	2.690	
Mean serum ferritin				
6-10	50	3005.90	1587.091	0.474
11-15	16	3343.06	1766.621	

Table 4: Comparison of mean TSH for duration of blood transfusion

Duration of blood transfusion	**n**	**Mean**	**Std. Deviation**	**P value**
Mean TSH				
5-10	53	3.676	2.116	0.343
11-15	13	4.350	2.897	
Mean serum ferritin				
5-10	53	3089.09	1587.259	0.988
11-15	13	3081.69	1839.551	

DISCUSSION

Thyroid hormones are important for the proper development, differentiation and metabolism of cells. Thyroid dysfunction has been reported in a number of studies on thalassemia patients. A wide range of pathogenic mechanisms may be involved. Tissue chronic hypoxia and iron overload have a direct toxic effect on the thyroid gland[8]. High concentrations of labile plasma iron and labile cell iron may lead to the formation of free radicals and the production of reactive oxygen species resulting in cell and organ damage[9]. In severe iron overloaded thalassemic patients the anterior pituitary may also be damaged and regulatory hormonal secretion (LH, FSH, and TSH) may be disrupted[10]. Organ siderosis (liver, cardiac and skeletal muscle, kidney) may affect specific receptors, which regulate thyroid hormone action and convert T4 to the bioactive T3.

In present study mean age of thalassemic patients was 8.73±2.569 years, mean serum TSH was 3.8085±2.281 µIU/ml, mean serum ferritin was 3087.64±1.625ng/dl.

In one study Malik et al[1] mean age of thalassemic patients was 7.6±2.5 years which is comparable with our study. Similar mean age (7.65 ± 3.61) of thalassemic patients was also reported by Karim et al[11] in their study.In present study male patients were 65% and female patients were 35%. Similar results were reported by Karim et al[11] in their study.

Solanki et al[12] reported mean serum TSH and mean serum ferritin as 7.14±9.04 and 2927.40±783.39 which is comparable with the findings of my study.

In present study negative correlation was noted between serum TSH and serum ferritin which was statistically insignificant (r=-0.014, P= 0.911). Solanki et al[12] also reported that there was no correlation between serum TSH and serum ferritin level (P-value= 0.38). Farooq MS et al[13] also reported negative correlation between serum ferritin and serum TSH which was statistically insignificant. Garadah TS et al[14] in their study reported that higher serum TSH levels of the patients of β thalassemia major correlated positively with the levels of serum Ferritin (r=0.34, p=0.014) results of this sudy are not supporting my study. Eshragi et al[4] also reported a Correlation between TSH and serum ferritin level which was not significant (p=0.584)

In present study mean serum TSH in male and female patients was 3.820±2.219 µIU/ml and 3.787±2.442µIU/ml respectively. Comparison of mean serum TSH between male and female patients was done and insignificant (P=0.956) difference between mean TSH of male and female patients was noted. Farooq MS et al[13] mean serum TSH in male and female patients as 3.67± 0.69 and 4.73±1.20 and the different statistically insignificant p value 0.143. Findings of this study are comparable with our findings. In present study mean serum ferritin levelin

male and female patients was 3296.44±1752.368 ng/dl and 2697.26±1301.453 ng/dl respectively and insignificant (P=0.155) difference between serum ferritin levelof male and female patients was noted. Irshaid et al[15] reported serum ferritin level in male and female patients as 2699±858 and 2412±750 which is comparable with my study.

CONCLUSION

Results of this study revealed that there is negative correlation between serum TSH and serum ferritin levels which was statistically insignificant. Results of this study also showed insignificant difference between mean serum TSH and mean serum ferritin levels of male and female patients were observed.

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