Original article:

Study of thyroid hormone status in patients of iron deficiency anemia

[1]Dr.Jayita Debnath , [2]Dr. (Mrs.) Vaishali Dhat , [3]Dr. (Mrs) M. A. Tilak

[1]PG.MD Biochemistry,

[2]Professor, Department of Biochemistry,

[3]Professor and Head, Department of Biochemistry

Department of Biochemistry,

DR. D. Y. Patil Medical College, Hospital and Research Centre, Pimpri, Pune – 411018.

Corresponding author: Dr.Jayita Debnath

Abstract:

Introduction: Iron deficiency in addition to anemia, results in the depletion of iron-dependent intracellular enzymes participating in many metabolic pathways.Hypothyroidism also is a major health issue affecting three to ten percent of adults.Several minerals and trace elements like iodine, iron, selenium & zinc are essential for normal thyroid hormone metabolism.

Aim: In some studies, thyroid hormone metabolism has been reported to be disturbed in iron deficiency. So the present study is designed to assess the effects of iron deficiency on thyroid hormonal activity.

Material and Method: The Institutional Ethical Committee clearance was obtained before commencement of the study. An informed consent was obtained from the participants of the study. 120 subjects between the age group of 18 to 45 years were included in the study(60 clinically diagnosed patients of iron deficiency anaemia were taken as cases and60 healthy age and sex matched subjects were taken as controls).Hb,MCV, MCH, MCHC, Serum ferritin,Serum iron,TIBC,SerumT3, SerumT4,TSH were estimated in all the participants.

Results: This study showed that the serum TSH levels are significantly higher in cases compared to controls. Though serum T3 and T4 levels are within normal range in both cases and controls but there is a significant decrease in mean T3 and T4 in cases as compared to controls .This study also showed a negative correlation of serum ferritin with serum TSH and that was statistically significant and also there was a significant positive correlation between serum ferritin and serumT3 and T4 levels.

Conclusion: Based on our study results it can be concluded that iron deficiency decreases TPO activity, which decreases circulating thyroid hormone(T3,T4) concentrations and increase TSH levels.

Key words: Iron deficiency, anemia, thyroid hormone.

Introduction:

Iron deficiency is one of the most prevalent nutrient deficiencies in the world, affecting an estimated two billion people[(1)], and half of the anemia is due to iron deficiency[(2).] Iron deficiency results in the depletion of iron-dependent intracellular enzymes participating in many metabolic pathways. Since iron is essential for all cells, many systems are affected in iron deficiency in addition to anemia. Thyroid dysfunction is a common endocrine disorder affecting about 300 million people worldwide[(3)]. Particularly hypothyroidism affects between three and ten per cent of adults, with incidence higher in the elderly and women [(4)].Several minerals and trace elements like iodine, iron, selenium &zinc are essential for both synthesis and metabolism of thyroid hormones . Erdem Gökdeniz et al studied the effects of iron deficiency anemia on the thyroid functions. Secondary and subclinical hypothyroidism was found in iron deficiency anemia. Hormonal changes returned to normal values with iron supplementation [(5)].Discrepant views are also shown by some studies. The survey in Turkey by Yavuz et al [(6)] showed no correlation between iron status and thyroid hormone levels in school children.

As iron deficiency is one of the most overlooked causes of thyroid dysfunction and results of the studies on "effects of iron deficiency anaemia on thyroid function" are contradictory, the present study is designed to assess the effects of iron deficiency on thyroid hormonal activity.

Aim:

The aim of this study was to find out the effect of iron deficiency anemia on thyroid hormonal activity.

Objectives:

1. To estimate blood hemoglobin, serum iron, TIBC, serum ferritin, MCV, MCH, MCHC in cases and controls.
2. To estimate serum levels of thyroid hormones like T3,T4, TSH in cases and controls.
3. To find out correlation between iron deficiency anemia and thyroid hormone profile.

Material and methods:

The current prospective cross sectional study was conducted in Department of Biochemistry, Dr.D.Y.Patil Medical College, Pimpri, Pune-18.

The Institutional Ethical Committee clearance was obtained before commencement of the study. An informed consent was obtained from the participants of the study. The study was conducted between July 2015 to September 2017.

Inclusion criteria:120 subjects between the age group of 18 to 45 years were included in the study and they were divided into two groups-60 clinically diagnosed patients of iron deficiency anaemia were taken as cases and60 healthy age and sex matched subjects were taken as controls.

Exclusion criteria:Participants not willing for consent, Patients having pregnancy, Patients having known thyroid disorder, and positive for Anti-TPO and Anti-TG,Diabetes mellitus,Hypertension,Hepatic disorder ,Heart diseases,Renal diseases.

Laboratory investigations:

For the diagnosis of iron deficiency anaemia Hb,MCV,MCH,MCHC,Serum ferritin,Serum iron,TIBC were estimated.To evaluate the thyroid hormone status SerumT3,SerumT4,TSH were estimated.

Methods:

Haematological examinations were done in BENESPHERA 5-part haematology analyser[7].Thyroid profile was done by Chemiluminescence immunoassay(CLIA) in MonobindIncAutoplex machine[8].Serum ferritinwas done by ELISA Method in MonobindIncAutoplexmachine[9].Serum iron and TIBC were done by Ferrozin method in Cobas C 311 machine[9,10].

Statistical method: The sample size was determined by using primer of biostatistics. Data is entered in MS excel file and statistical analysis is done by using SPSS version 20 by "unpaired t" test and Mann-Whitney U test, Chi-square test. Pearson's Correlation coefficient is used to find out the correlation.

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

Results:

The variation in age and gender distribution of the study population are statistically insignificant(p-value >0.05), hence the two groups are comparable for the study.

Fig:1: Comparison between the parameters of iron deficiency anemia among cases and controls.

	MEAN±SD						
	Hb (g/dl)	MCV (fl)	MCH (pg)	MCHC (gm/dl)	S.IRON (µg/dl)	TIBC (µg/dl)	FERRITIN (ng/ml)
cases	7.70±2.07	68.79± 8.49	20.35± 5.44	27.74± 5.66	42.75± 35.47	398.20± 133.73	13.92± 10.34
control	13.05± 1.03	94.42± 7.05	28.91± 2.64	30.71± 1.57	89.13± 32.95	349.76± 59.11	55.20± 32.78
P-VALUE	<0.001	<0.001	<0.001	<0.001	<0.001	0.012	<0.001

[Reference range**:**Hb:13-17 g/dl (male),12-15 g/dl(female)**;**MCV:80-100 fl;MCH:27-32 pg, MCHC: 31.5-34.5;TIBC: 215-535µg/dl**, S**erum iron:60-180 µg/dl; Serum ferritin-10-291 ng/ml (women),22-322 ng/ml(MEN).]

As can be seen in fig:1the mean hemoglobin concentration is very low in cases as compared to the controls. The differences between mean MCV,MCH,MCHC in cases and controls arestatistically significant.The differences between mean serum ferritin ,TIBC, serum iron in cases and controls are statistically significant.

Fig:2: Comparison between the levels of thyroid hormones among cases and controls.

	MEAN±SD		
	T3(ng/ml)	T4(µg/dl)	TSH(mIU/ml)
Cases	1.03±0.37	6.40±2.44	28.42±27.83
Control	1.42±0.92	9.01±2.30	2.58±2.38
P value	0.004	<0.001	<0.001

[Reference range:T3:0.5-1.85ng/ml;T4:4.8-11.6µg/dl;TSH:0.5-6.05mIu/ml]

As seen in fig 2,There is significant difference between mean T3,T4,TSH in cases and controls.

Fig:3:Correlationbetween serum ferritin and serum T3 levels.

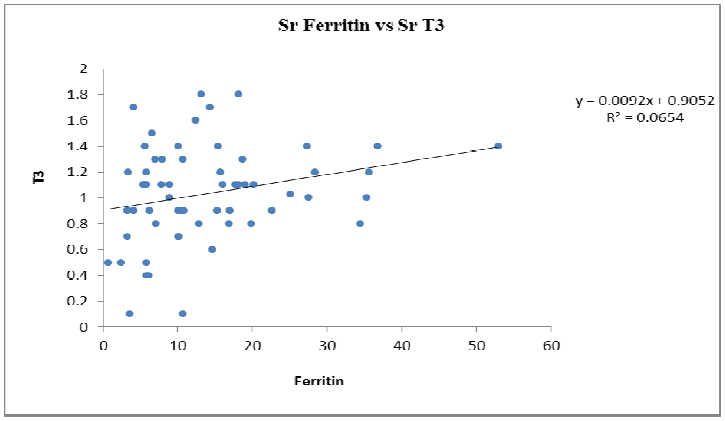


Fig:4: Correlation between serum ferritin and serum T4 levels.

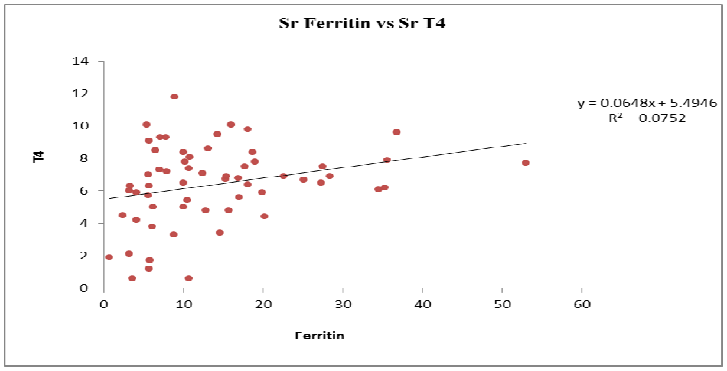
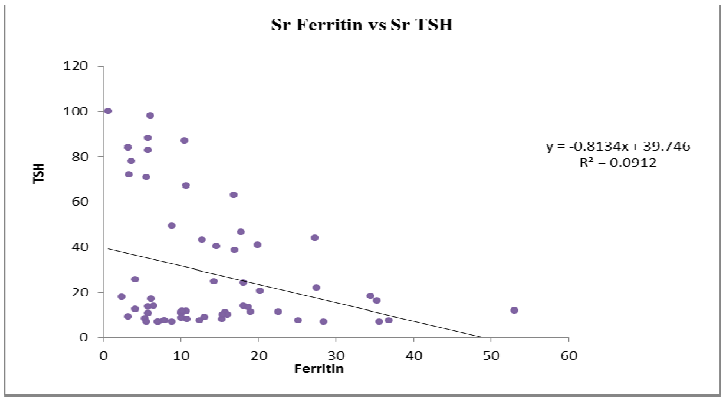


Fig 3 and 4 show that serum T3 and T4 has significant positive correlation with serum ferritin .

Fig:5:Correlation between serum ferritin and serum TSH levels



Discussion:

Iron is an essential element for many living organisms .Since it is necessary for structure and function of many enzymes, many systems are affected in its deficiency. In the present study we explored the effects of iron deficiency anemia in thyroid hormone status.

This study showed that the serum TSH levels are significantly higher in cases compared to controls ($p<0.001$).Iron dependent thyroperoxidase (TPO) catalyzes first two steps of thyroid hormone synthesis (iodination of thyroglobulin and coupling of the iodotyrosine residues).Iron deficiency may lower thyroperoxidase activity as it is an iron dependent enzyme and interfere with the synthesis of thyroid hormones causing decreased levels of circulating thyroid hormones (T3, T4) and increased TSH levels. This result is in accordance with a study done by T.V.K Padmaja et.al [(11)] and another study done by Blum And Blum [(12)]. Hess and his co-workers showed in their study that thyroid peroxidase activity is significantly reduced in iron deficiency anaemia[(13)].The present study showed that the serum T3 and T4 levels are within normal range in cases as well as in the healthy subjects. But there is a significant decrease in mean T3 and T4 in cases as compared to controls ($p<0.05$) though they are within normal range. Iron deficiency slows turnover of T3 and may reduce T3 nuclear binding. Iron deficiency anemia decreases serum T3 and T4 by reducing peripheral conversion of T4 to T3 and increasing TSH concentration [(14)].Michael B. Zimmermann et al in their study, found higher TSH and lower total T4 concentration in poor maternal iron status[(15)].The present study showed a negative correlation of serum ferritin with serum TSH and that was statistically significant ($p <0.05$) and also there was a significant positive correlation between serum ferritin and serumT3 and T4 levels ($p <0.05$).Though low hemoglobin concentration is most the most important sign of anemia, a significant fall in circulating hemoglobin cannot be detected until the final stage of iron deficiency [(16)]. Serum ferritin is a measure of iron stores and is the best single test to confirm iron deficiency. Iron deficiency lowers TPO activity and this will decrease circulating thyroid hormone concentration and increase TSH levels as reflected by the negative correlation between ferritin and TSH levels[(11)].This result is consistent with a study done by Mohammad Hassan Eftekhari et al.They found a significant negative correlation between the ferritin concentration and TSH levels[(17)].Hess et al have suggested that iron deficiency prevent T4 to T3 conversion by reducing hepatic thyroxine deiodinase activity [(13)].These researchers have suggested that iron deficiency anemia changes thyroid metabolism by reduced oxygen transport and hypoxia, changing the impact on the metabolism of central nervous system or leading to modification of T3 binding capacity. Also iron dependent peroxidase which catalyzes the transfer of iodine to thyroglobulin is sensitive to decrease in iron level. A considerable amount of data indicates that iron deficiency impairs thyroid metabolism, lowers serum T3, T4 and increases TSH levels in iron deficient humans [(15)]. Subjects with lower iron stores are shown to have higher reverse T3 concentration[(18)].

Further studies on large sample size need to be carried out to assess the effect of iron supplements insuch patients.

Conclusion:

Based on our study results it can be concluded that iron deficiency decreases TPO activity, which decreases circulating thyroid hormone(T3,T4) concentrations and increase TSH levels. Seeing the results of our study, we suggest thyroid hormone status evaluation in all the patients of iron deficiency anemia. If abnormal thyroid profile is detected in patients of iron deficiency anemia , supplementation of iron at an early stage may be beneficial to improve the thyroid hormone status .

Acknowledgement:

I am really thankful department of Biochemistry, Dr.D.Y.Patil Medical college for supporting me to complete this study. I am indebted to all those patients who made the backbone of the study.

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