DOI: 10.7860/NJLM/2022/48551.2556

Original Article

Biochemistry Section

Relationship between Iron Profile and Thyroid Profile in Hypothyroid Patients

SANTOSH KUMAR[1], JIUT RAM KESHARI[2], REKHA KUMARI[3], PRITAM PRAKASH[4], UDAY KUMAR[5], VED PRAKASH[6]

ABSTRACT

Introduction: Thyroid hormone biosynthesis is dependent on iron metabolism. Changes in iron metabolism and its deficiency may cause a change in the profile of thyroid hormone. Such interferences caused can lead to hypothyroidism in case of anaemia or the other way round.

Aim: To find a relationship between various parameters of iron profile to that of thyroid profile in hypothyroid patients when compared to normal healthy subjects.

Materials and Methods: Present case-control study was conducted on 50 hypothyroid patients and 50 healthy subjects of same age, in the Department of Endocrinology, IGIMS, Patna between April 2017 to June 2018. Serum ferritin and Serum T3, T4, and Thyroid Stimulating Hormone (TSH) were estimated by Chemiluminescence Immuno Assay (CLIA) method. Serum iron estimation was done using TPTZ (2,4,6-Tripyridyl-s-triazine) method and Total Iron Binding Capacity (TIBC) estimation was done by Nitroso PSAP method. All statistical test and analysis were performed in Statistical Package for the Social Science (SPSS) 16.0. The differences between mean values of groups for each test variable were tested by Student's t-test after testing for homogeneity of variance and normality test (Kolmogorov-Smirnov test).

Results: The mean age of the hypothyroid patients was 30.28±10.5 years while it was 31.14±10.4 years in control group. It was observed from the study that mean serum ferritin level and iron level were significantly lower in hypothyroid subjects compared to control groups ($p<0.001$) while TIBC was significantly higher ($p<0.001$). Serum ferritin and iron were found to be negatively correlated with TSH (-0.695 and -0.541) and positively correlated to T3 and T4, respectively.

Conclusion: Evaluating iron profile in thyroid disorder may be an aid to the treatment modality and disease outcome.

Keywords: Ferritin, Hypothyroidism, Thyroid hormones

INTRODUCTION

Thyroid related diseases burden in our country is a menace. Hypothyroidism can be complicated by many disease, one such underlying disorder can be iron metabolism related disorder [1]. Previous studies have shown that for proper functioning of thyroid hormone various minerals and trace elements are required and iron is one of the important element involved in the metabolism of thyroid hormone [2]. Iron act asa co-factor in catalysis of various biological enzymes including Thyroid Peroxidase (TPO) [3]. Thyroid peroxidase enzyme is involved in catalysis of the two important reaction of thyroid hormone biosynthesis [4]. First, it acts as a membrane bound enzyme responsible for the oxidation of iodide and secondly, it helps in binding of iodine to tyrosyl residue of thyroglobulin [5].

Deficiency of iron may cause changes in thyroid hormone status in patients. Ferritin corresponds to body iron stores and in hypothyroidism its serum levels is altered [6]. Exact mechanism of whether iron levels interfere with thyroid hormone synthesis or a hypothyroid state leads to altered iron profile is not clear and yet to be evaluated. Poor gut absorption of iron could occur in hypothyroidism [7,8]. Monitoring iron profile in hypothyroid patients can aid the treatment protocol and outcome of the disease. This study aimed to find the relationship between various parameters in iron profile to that of thyroid profile in hypothyroid patients when compared to normal healthy subjects.

MATERIALS AND METHODS

This case-control study was conducted on patients attending the Department of Endocrinology Indira Gandhi Institute of Medical Science, Patna between April 2017 to June 2018 after obtaining ethical clearance from Indira Gandhi Institute of Medical Sciences (IGIMS) Ethical Committee. Patient informed consent was taken before including them in the study. A total of 100 subjects were taken with age ranging from 18-70 years of which 50 were healthy individual comprising the control group and 50 hypothyroid patients newly diagnosed were grouped as cases. There were 37 females and 13 males in case group while 34 females and 16 males were in the control group.

Inclusion criteria: All clinically hypothyroid patients of age group between 18-70 years and of both sexes were included in the study.

Exclusion criteria: Extremes of age below 18 years and above 70 years, people with other endocrinopathies, chronic renal disease, chronic infections, patients taking iron supplement, subclinical hypothyroidism, patients on blood transfusion and pregnant subjects were excluded from the study.

T3, T4, TSH, Serum ferritin, Serum iron and TIBC levels were evaluated in both groups. About 10 mL of venous blood was collected from both study and control groups in fasting condition in the morning hours. Blood was allowed to clot at the room temperature for atleast 30 minutes. Then, it was centrifuged at 2000 rpm for 10 minutes. Within two hours of centrifugation serum was transferred by pipette into another tube and tightly stoppered. The extracted serum samples were stored at 2 to 8°C laboratory refrigerator (RLR-300, REMI). The clear serum was analysed within eight hours. Serum ferritin and serum T3, T4, and TSH were estimated by CLIA method in Beckman Coulter Access 2 instrument. Serum iron estimation was done using TPTZ (2,4,6-Tripyridyl-s-triazine) method (Beckman coulter). TIBC estimation was done by Nitroso PSAP method (Beckman coulter). Both the test was done on AU400 chemistry analyser (Olympus, Beckman coulter, USA) [9].

STATISTICAL ANALYSIS

All statistical test and analysis were performed in SPSS 16.0. The differences between mean values of groups for each test variable were tested by Student's t-test after testing for homogeneity of variance and normality test (Kolmogorov-Smirnov). The correlations between serum ferritin, TIBC, iron and T3, T4, TSH were presented by Pearson's correlation coefficient (r) for each pair. Results were interpreted at level of 95% confidence interval.

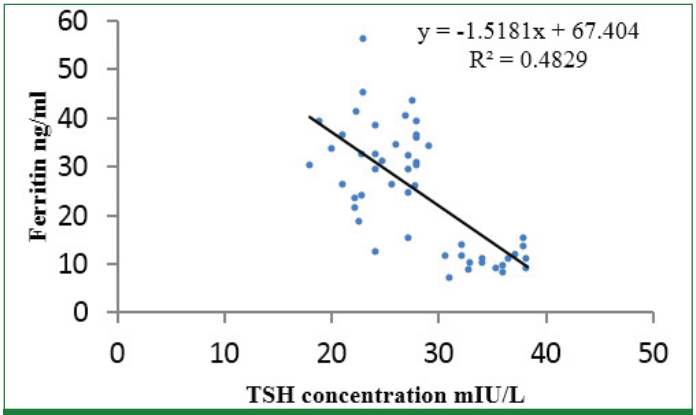
RESULTS

In the control group, there were 34 females and 16 males while that among hypothyroid cases 37 were females and 13 were males. The mean age of the hypothyroid patients was 30.28±10.5 years while it was 31.14±10.4 years in control group. Means of various thyroid and iron profile parameters in case and control group were compared using independent t-test assuming the normality and homogeneity of variance of the data. All the results have been summarised in [Table/Fig-1].

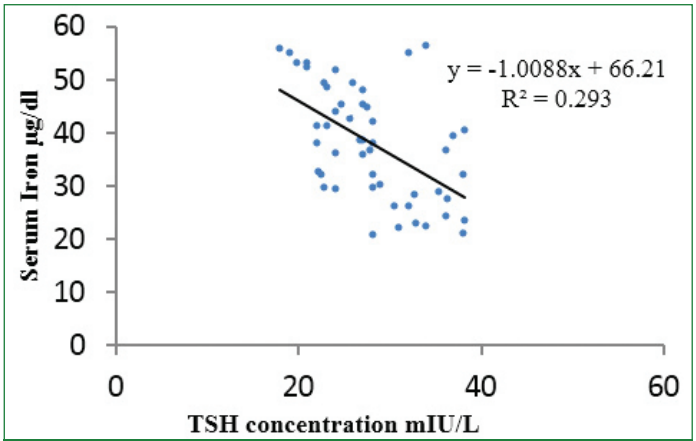
Test parameter	Control group Mean±SD (Range)	Case group Mean±SD (Range)	p-value
T3 (ng/mL)	1.45±0.27 (0.76-1.86)	0.48±0.24 (0.19-1.1)	<0.001
T4 (µg/dL)	8.11±1.58 (5-10.4)	2.79±1.00 (1.4-4.8)	<0.001
TSH (mIU/L)	2.96±0.84 (1.73-4.6)	28.04±5.63 (18-38.2)	<0.001
Ferritin (ng/mL)	38.29±6.38 (23.4-49.4)	24.83±12.30 (7.36-56.1)	<0.001
Iron (µg/dL)	72.45±9.27 (59.3-102)	37.92±10.50 (20.67-56.2)	<0.001
TIBC (µg/dL)	248.11±51.32 (114-322)	293.17±72.16 (192-472)	<0.001

[Table/Fig-1]: Comparing the various thyroid parameters and iron profile parameters in control and case group.
p-value <0.05 considered significant

Ferritin was strongly negatively correlated with TSH (r=-0.695) in hypothyroid case group [Table/Fig-2]. A positive and significant correlation was observed between iron and T3 as well as T4 while a moderately negative correlation was seen between iron and TSH (r=-0.541) in hypothyroid case group [Table/Fig-3,4]. A similar observation like serum iron for T3 and T4 was found with ferritin in hypothyroid patients. TIBC was not significantly correlated with TSH (r=0.178, p>0.05) in hypothyroid cases [Table/Fig-4].



[Table/Fig-2]: Scatter plot showing correlation between Ferritin and TSH (r=-0.695).



[Table/Fig-3]: Scatter plot showing correlation between Serum Iron and TSH (r=-0.541).

Parameters compared	Pearson's correlation coefficient r	p-value
Ferritin and T3	0.377	<0.05
Serum Iron and T3	0.305	<0.05
TIBC and T3	-0.397	<0.05
Ferritin and T4	0.387	<0.05
Serum Iron and T4	0.293	<0.05
TIBC and T4	-0.05	>0.05
Ferritin and TSH	-0.695	<0.05
Serum Iron and TSH	-0.541	<0.05
TIBC and TSH	0.178	>0.05

[Table/Fig-4]: Showing the correlation between various thyroid parameters and iron profile parameters case group.
p-value <0.05 considered significant

DISCUSSION

It was observed from the study that mean serum ferritin level and iron were significantly low in hypothyroid subjects when compared with control groups while TIBC was significantly higher. There was a positive and a significant correlation of serum ferritin with both T3 and T4 in hypothyroid patients. A negative and highly significant correlation between ferritin and Thyroid Stimulating Hormone (TSH) in hypothyroid patients was found. Similar correlation pattern was observed for serum iron and above thyroid function parameters in hypothyroid case group. The correlation of TSH was found to be weakly positive but insignificant with TIBC in the hypothyroid cases. Level of T4 with TIBC were not significantly correlated in hypothyroid case group. There was negative correlation of T3 with TIBC in hypothyroid case group. Previous studies also reported similar findings in animals and human beings Hess SY et al., conducted experimental studies on TPO activity in rats and concluded that its activity is greatly reduced in the group of rats fed with iron deficient diet [10]. This finding supports what authors have observed as hypothyroid patients were mostly iron deficient.

Some studies linked thyroid function and hematopoiesis. Christ-Crain M et al., reported external intake of thyroxine increases the rate of erythropoiesis by increasing the level of erythropoietin, which leads to increased iron demand [11]. Erdogan M et al., observed an increase in occurrence of microcytic hypochromicanaemia in clinical and subclinical cases of hypothyroidismas compared to controls [12]. There were some studies to describe the role of reverse T3 hormone (rT3) and iron metabolism. Eftekhari MS et al., study provided support for the contention that the decrease in rT3 is related to changes in iron status. In their study, iron supplementation and improved iron status caused the plasma level of rT3 to significantly decrease in the iron with iodine and iron supplement groups. [13]. Some other studies have established the inverse correlation between Haemoglobin (Hb) and thyroid hormonestatus. Bremner AP et al., found the significant association between free T3 and Hb and inverse relationship of TSH with serum iron and transferrin saturation [14]. Bivolarska A et al., reported a significant association between T4 level and Hb [15]. These studies indicate the involvement of thyroid hormone in erythropoiesis. A study by Yavuz O et al., dismissed any association between thyroid hormone and iron [16].

There were studies which reported that iron deficiency may be associated with low levels of thyroid hormones [5,12,17]. These studies have similar findings as with present study. The underlying mechanism of interference of low ferritin level in hypothyroidism is yet to be evaluated. A possible connection to such interference may be related to implication of iron dependent thyroperoxidase enzyme needed for biosynthesis of thyroid hormone. Studies on children also suggest that the similar association of hypothyroidism and disorder in iron metabolism [18,19]. Thus, it can be concluded that estimation of iron profile may be of significance in patients with hypothyroidism as it may be helpful in the treatment and monitoring of the disease.

Limitation(s)

This study was conducted upon a relatively small group of population that is not quite enough to establish a firm association between thyroid profile and iron profile in hypothyroids. Another limitation is lack of assessment of anti-Thyroid Peroxidase Antibody (anti-TPO) in this study for exclusion of autoimmune thyroid disorders and to look for its association in iron deficient subject group. Also, this study does not include the level of haemoglobin and its association with transferrin saturation.

CONCLUSION(S)

The present study has tried to establish the association between iron status and thyroid profile in an adult population and it has been noticed that the patient having abnormal thyroid profile (low level of thyroid hormone as in hypothyroid patients) shows altered status of iron profile in blood and iron store. As there will always be some shortcoming in a small sample size based study, authors have taken it as a future scope to carry forward this study in a large group of population that also include pregnant females and children with an estimation of haemoglobin, anti-TPO antibodies and transferring saturation, which can account for firm association of thyroid hormones and iron levels altered status in hypothyroids. Also, further studies are required to establish ferritin or iron to be an important and independent predictor of hypothyroidism.

REFERENCES

[1] Beard J, Tobin B, Green W. Evidence of thyroid hormone deficiency in iron-deficient anemic rats. J Nutr. 1989;119:772-78.
[2] Metwalley KA, Farghaly HS, Hassan AF. Thyroid status in Egyptian primary school children with iron deficiency anemia: Relationship to intellectual function. Thyroid Res Pract. 2013;10:91-95.
[3] Kammal M, Abdrabo AA. Assessment of thyroid hormone levels in Sudanese females with iron deficiency. Sudan Med J. 2014;50(2):98-102.
[4] Carvalho DP, Dupuy C. Thyroid hormone biosynthesis and release. Mol Cell Endocrinol. 2017;458:06-15.
[5] Akhter S, Nahar ZU, Parvin S, Alam A, Sharmin S, Arslan MI. Thyroid status in patients with low serum ferritin level. Bangladesh J Med Biochem. 2012;5:05-11.
[6] Dahiya K, Verma M, Dhankhar R, Ghalaut V, Ghalaut PS, Sachdeva A. Thyroid profile and iron metabolism: mutual relationship in hypothyroidism. Biomedical Research. 2016;27(4):1212-15.
[7] Donati RM, Fletcher JW, Warnecke MA, Gallagher NI. Erythropoiesis in hypothyroidism. proceedings of the society for experimental biology and medicine. 1973;144(1):78-82.
[8] Chandel RS, Chatterjee G, Abichandani LG. Impact of subclinical hypothyroidism on iron status and hematological parameters. Ann Pathol Lab Med. 2015;2: 21-25.
[9] Dupuy AM, Debarge L, Poulain M, Badiou S, Rossi M, Cristol JP. Determination of serum ferritin using immunoturbidimetry or chemiluminescent detection in comparison with radioimmunoassay- a compendium of a methodological juxtaposition. Clin Lab. 2009;55: 207-15.
[10] Hess SY, Zimmermann MB, Arnold M, Langhans W, Hurrell RF. Iron deficiency anemia reduces thyroid peroxidase activity in rats. J Nutr. 2002;132:1951-55.
[11] Christ-Crain M, Meier C, Huber P, Zunewski H, Stabb JJ, Muller B, et al. Effect of restoration of euthyroidism on peripheral blood cells and erythropoietin in women with subclinical hypothyroidism. Hormones (Athens). 2003;2:237-42.
[12] Erdogan M, Kosenli A, Sencer G, Kulaksizoglu M. Characteristics of anemia in subclinical and overt hypothyroid patients. Endocr J. 2012;59:213-20.
[13] Eftekhari MS, Keshavarz SA, Jalali M, Elguero E , Eshraghian MR, Simondon KB. The relationship between iron status and thyroid hormone concentration in iron-deficient adolescent Iranian girls. Asia Pac J Clin Nutr. 2006;15(1):50-55.
[14] Bremner AP, Feddema P, Joske DJ, Leedman PJ, Leary PC O, Olynyk JK, et al. Significant association between thyroid hormones and erythrocyte indices in euthyroid subjects. Clin Endocrinol (Oxf). 2012;76(2):304-11.
[15] Bivolarska A, Gatseva P, Maneva A. Association between thyroid and iron status of pregnant women in Southern Bulgaria. J Endocrinol Diabetes Mellit. 2013;1:15-21.
[16] Yavuz O, Yavuz T, Kahraman C, Yesildal N, Bundak R. The relationship between iron status and thyroid hormones in adolescents living in an iodine deficient area. J Pediatr Endocrinol Metab. 2004;17(10):1443-49.
[17] Das C, Sahana PK, Sengupta N, Giri D, Roy M, Mukhopadhyay P. Etiology of anemia in primary hypothyroid subjects in a tertiary care center in Eastern India. Indian J Endocr Metab 2012;16(Suppl S2):361-63.
[18] Khatiwada S, Lamsal M, Gelal B, Gautam S, Nepal AK, Brodie D, et al. Anemia, iron deficiency and iodine deficiency among Nepalese school children. Indian J Pediatr. 2016;83:617-21.
[19] Tienboon P, Unachak K. Iron deficiency anaemia in childhood and thyroid function. Asia Pac J Clin Nutr. 2003;12:198-202.

PARTICULARS OF CONTRIBUTORS:
1. Senior Resident, Department of Biochemistry, Indira Gandhi Institute of Medical Sciences, Patna, Bihar, India.
2. Additional Professor, Department of Biochemistry, Indira Gandhi Institute of Medical Sciences, Patna, Bihar, India.
3. Additional Professor and Head, Department of Biochemistry, Indira Gandhi Institute of Medical Sciences, Patna, Bihar, India.
4. Assistant Professor, Department of Biochemistry, Indira Gandhi Institute of Medical Sciences, Patna, Bihar, India.
5. Professor, Department of Biochemistry, Netaji Subhas Medical College, Patna, Bihar, India.
6. Associate Professor, Department of Endocrinology, Indira Gandhi Institute of Medical Sciences, Patna, Bihar, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Pritam Prakash,
Assistant Professor, Department of Biochemistry, Indira Gandhi Institute of Medical Sciences, Sheikhpura, Patna-800014, Bihar, India.
E-mail: pritamprakash.2050@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Mar 03, 2021
- Manual Googling: May 20, 2021
- iThenticate Software: Sep 07, 2021 (19%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Jan 16, 2021**
Date of Peer Review: **Mar 04, 2021**
Date of Acceptance: **May 27, 2021**
Date of Publishing: **Jan 01, 2022**