e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2023; 15(9); 967-970

Original Research Article

Serum Levels of Iron Profile and Ceruloplasmin in Hypothyroid Patients and Normal Individuals: A Case Control Study

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Received: 25-06-2023 / Revised: 28-07-2023 / Accepted: 30-08-2023

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Conflict of interest: Nil

Abstract:

Background: Metabolism of thyroid hormones and iron is quite interdependent. Deficiency of iron can produce hypothyroidism and vice versa. Ceruloplasmin (Cp) is considered as a protective antioxidant due to its ability to react and scavenge free radicals.

Objectives: To evaluate and to compare the serum levels of Iron, Total iron binding capacity (TIBC) and Ceruloplasmin in hypothyroid patients and normal individuals.

Methodology: In this study we have taken a group of 50 clinically proven hypothyroid cases diagnosed by thyroid profile and an equal number of ages and sex matched healthy subjects. After taking written informed consent the fasting venous blood sample was drawn from both the controls and cases for the assay of Iron and TIBC by Ferrozine method and serum Ceruloplasmin by Nephelometry method.

Results: A significant decrease in serum Iron and ceruloplasmin and increase in serum TIBC was seen in hypothyroid patients compared to normal subjects. (p value < 0.001).

Conclusion: The present study establishes Iron, TIBC and Ceruloplasmin are useful biomarkers of oxidative stress in hypothyroidism.

Keywords: Hypothyroidism, Iron, TIBC, Ceruloplasmin.

Introduction

Multiple micronutrient deficiencies are still a major public health problem faced by developing countries. Deficiencies of trace elements like iodine, iron, zinc and selenium also impair thyroid function. [1] Iron deficiency has multiple adverse effects on thyroid metabolism. It decreases circulating thyroid hormone concentration. [2] Metabolism of thyroid hormones and iron is quite inter-dependent. Iron metabolism is very intricately connected to thyroid hormone metabolism. Estimation of serum ferritin (storage form), iron and total iron binding capacity (TIBC), which measures percent saturation of transport form transferrin with iron, may be of great significance in hypothyroidism. [3] Ceruloplasmin is a α_2-Globulin that contains approximately 95% of the total copper found in serum. The primary physiological role of Cp involves plasma redox reactions. Ceruloplasmin is also important in the control of membrane lipid oxidation – probably by direct oxidation of cations – thus preventing their catalysis of lipid peroxidation. Ceruloplasmin is a major defense against harmful effects of ROS in cells and in cultured erythrocytes, with a high capacity to degrade exogenous hydrogen peroxide in hypothyroidism. [4]

Presently oxidative stress is considered as an important pathogenic mechanism in so many different diseases. In hypothyroidism there is an imbalance in thyroid hormones which leads to production of reactive oxygen species and concomitant use of antioxidants. There are several biochemical markers showing the extent of on-going oxidative stress in the body.

Our objective was to estimate serum iron, total iron binding capacity (TIBC) and ceruloplasmin in hypothyroid patients may be of great significance in to assess oxidative stress and antioxidant activity.

Material and Methods

A case control study of serum iron, TIBC and ceruloplasmin was carried out in patients with hypothyroid and controls. After obtaining institutional ethical clearance the study was carried out in clinically proven cases of hypothyroidism and age and sex matched healthy individuals as controls from medicine outpatient department of Subbaiah hospital attached to Subbaiah institute of medical sciences, Shimoga.

A total number of 50 patients with hypothyroidism and an equal number of controls were selected based on inclusion and exclusion criteria for the present study. The patients and controls voluntarily participated in the study.

Inclusion criteria:

- Clinically proven cases of Hypothyroidism by thyroid profile with the age group of 30-70 years.
- An equal number of age and sex matched healthy individuals were included.

Exclusion criteria: Hypothyroid patients with

- Hepatic and renal disease
- Sepsis and severe inflammatory diseases
- Anaemia, hemochromatosis, Wilson's disease
- Diabetes mellitus
- Chronic alcoholism are excluded from the study.

Method of sample collection:

After taking written informed consent about 5 ml of venous blood was drawn under aseptic conditions in a sterile bulb from selected subjects after a period of overnight fasting of 10-12 hours. Serum was immediately separated by centrifugation and used for analysis. Serum iron and TIBC was estimated by Ferrozine method and serum ceruloplasmin by Nephelometry method.

Statistical analysis:

Results were subjected for statistical analysis. Data thus obtained was expressed in terms of mean ± SD; proportions are analysed using independent student "t' test. p value ≤ 0.05 is considered as statistically significant.

Results

Table 1: Comparison of thyroid profile, Iron, TIBC and ceruloplasmin in controls, subclinical hypothyroidism and hypothyroidism

	Group -1 Control	Group-2 Subclinical Hypothyroidism	Group -3 Hypothyroidism	
Parameters	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	**p*- Value, Sig**
T3 (ng/dL)	2.02±0.44	1.6±0.29	0.9±0.2	p < 0.001 S
T4 (µg/dL)	8.4±1.8	6.9±1.6	2.9±0.9	p < 0.001 S
TSH (µIU/ml)	2.9±1.4	18.9±13.6	14.4±6.5	p < 0.001 S
Iron (µg/dL)	110.7± 23.9	106.5± 14.2	82.9±16.2	p < 0.001 S
TIBC (µg/dL)	291.6± 38.5	329.4± 35.1	351.8± 41.6	p < 0.001 S
Ceruloplasmin (mg/dL	37.7±9.7	30.8±6.6	27.4±8.1	p < 0.001 S

Table 2: Post-Hoc tests:

	Groups	**Tuckey HSD**
T3	Control and Subclinical hypothyroidism	p- value <0.001
	Control and hypothyroidism	p- value <0.001
	Subclinical hypothyroidism and hypothyroidism	p- value <0.001
T4	Control and Subclinical hypothyroidism	p- value = 0.001
	Control and hypothyroidism	p- value <0.001
	Subclinical hypothyroidism and hypothyroidism	p- value <0.001
TSH	Control and Subclinical hypothyroidism	p- value <0.001
	Control and hypothyroidism	p- value <0.001
	Subclinical hypothyroidism and hypothyroidism	p- value= 0.261
Iron	Control and Subclinical hypothyroidism	p- value= .659
	Control and hypothyroidism	p- value <.001
	Subclinical hypothyroidism and hypothyroidism	p- value <.001
TIBC	Control and Subclinical hypothyroidism	p- value= .001
	Control and hypothyroidism	p- value <.001
	Subclinical hypothyroidism and hypothyroidism	p- value= .069
Ceruloplasmin	Control and Subclinical hypothyroidism	p- value= .005
	Control and hypothyroidism	p- value <.001
	Subclinical hypothyroidism and hypothyroidism	p- value = .254

Discussion

Table 1 shows one way ANOVA was performed to compare the effect of three groups (Control, Subclinical hypothyroidism and hypothyroidism).

Test shows that there is a statistically significant difference in mean values of T3, T4, TSH, Iron, TIBC and Ceruloplasmin between at least two groups. [p- Value <.001]

Table 2 shows Post Hoc test using Tuckey's HSD test for multiple comparison found that there is a statistically significant difference in T3 and T4 between control and Subclinical hypothyroidism (p- value <.001), Control and hypothyroidism (p- value <.001) and Subclinical hypothyroidism and hypothyroidism (p- value <.001).

There is a statistically significant difference in TSH between control and Subclinical hypothyroidism (p- value <.001), Control and hypothyroidism (p- value <.001). There is no statistically significant difference in TSH between Subclinical hypothyroidism and hypothyroidism (p- value= 0.261).

In Iron between control and hypothyroidism (p- value <.001), subclinical hypothyroidism and hypothyroidism (p- value <.001) there is a statistical significance present. There is no statistically significant difference in Iron between control and subclinical hypothyroidism (p- value= 0.659).

In TIBC between control and hypothyroidism (p- value <.001) there is a statistical significance present. There is no statistically significant difference in Iron between control and subclinical hypothyroidism (p- value= 0.001), subclinical hypothyroidism and hypothyroidism (p- value 0.069).

In this study, iron was found to be decreased while that of TIBC to increase in patients suffering from hypothyroidism as compared to healthy controls. These results are in accordance with other studies which reported that iron deficiency may be associated with low levels of thyroid hormones. [5,6,7]

Metal ions, specifically iron, are necessary for the production of extremely reactive hydroxy radicals shifting the balance of body towards increased oxidative stress. [8] Increased oxidative stress has been reported in hypothyroidism and iron is a prominent player in this mechanism. [9,10] Thyroperoxidase, the key enzyme in thyroid hormone biosynthesis, is iron-dependent. Thus, iron deficiency may be the underlying cause in the development of hypothyroidism. This fact is of great significance while treating these patients. The symptoms of sympathetic overstimulation due to iron deficiency may worsen on administration of thyroxine. Thyroxine administration has been reported to increase erythropoietin levels and improve erythropoiesis. This leads to increased requirement of iron and may culminate in manifestations of iron deficiency. [11]

The correlation of TSH was found to be positive with TIBC while negative with iron showing an obvious association between thyroid hormones and iron metabolism. [12]

There is a statistically significant difference in Cp between Control and hypothyroidism (p- value <.001). There is no statistically significant difference in Cp between Subclinical hypothyroidism and hypothyroidism (p- value= 0.254), control and Subclinical hypothyroidism (p- value 0.005) in Post Hoc test shown in table 2.

Our finding is in accordance to the study done by Bhattacharya et al. [13] the primary physiological role of Cp involves plasma redox reactions. It can function as an oxidant or antioxidant depending on other factors, such as the presence of free ferric ions and ferritin binding sites. Ceruloplasmin is also important in the control of membrane lipid oxidation – probably by direct oxidation of cations – thus preventing their catalysis of lipid peroxidation. [8] Ceruloplasmin is a major defense against harmful effects of ROS in cells and in cultured erythrocytes, with a high capacity to degrade exogenous hydrogen peroxide. [4]

It has been suggested that hypothyroidism leads to oxidative stress and to a reduction of antioxidant defenses although the pathophysiological consequences of the decelerated antioxidant levels are not yet elucidated. This biochemical change is thought to be a physiological adaptation and a response to hypothyroidism. In agreement with previous findings, thyroid hormones are involved in combating the toxicity of oxidative stress in humans [10]. Thus, under normal conditions; the protective effect of thyroid hormone against oxidative stress can be explained by the function of antioxidants as a defense system. [14]

The depletion of antioxidants observed in hypothyroid individuals may reflect the increased free radical production in the electron transport chain in the mitochondrial inner membrane. The increase of free radicals is not compensated, as one would expect, due to a decrease of antioxidants like Ceruloplasmin. A high oxidative state in hypothyroid people has metabolic and biochemical characteristics such as increased mitochondrial enzyme activity. Thus, it is likely that patients' cells are damaged by prolonged oxidative stress that far exceeds the capacity of the patient's organs to synthesize antioxidant molecules or to synthesize them from extracellular sources. [15]

Conclusion

Thus, it can be concluded that estimation of iron profile and ceruloplasmin mandates in hypothyroid patients may be of significance in monitoring the disease. Simultaneous correction of both iron deficiency and hypothyroidism should be done as both effects each other's metabolism.

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