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SERUM FERRITIN LEVELS AND THYROID PROFILE: RELATIONSHIP IN HYPOTHYROIDISM

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ABSTRACT

The deficiency of micronutrients is one of the most important health problems seen in developing countries. Out of these, deficiency of iron presenting in the form of anemia, is very widespread in general population. The metabolism of iron is interrelated with the thyroid hormone metabolism, as iron is one of the components of some of the enzymes that take part in the thyroid hormone biosynthesis. The present study was conducted with the aim to estimate and compare the serum ferritin levels in patients with hypothyroidism and healthy controls. It was observed in our study that the serum ferritin levels were significantly decreased in hypothyroid patients as compared to normal healthy controls, which could be a manifestation of disturbed actions of iron-dependent enzymes leading to impairment in the metabolism of thyroid hormones. Thus, serum ferritin estimation could be useful for the evaluation of thyroid hormone action on the peripheral tissues.

INTRODUCTION

The deficiencies of various micronutrients are one of the most important public health problem faced by developing countries. Out of these, iron deficiency is very widespread in general population. The deficiency of trace elements like iron, iodine, zinc and selenium also hinders thyroid function. (1) A number of metabolic pathways and physiological components are influenced by thyroid hormones. (2) The metabolism of iron is convoluted to the metabolism of thyroid hormones. Iron is one of the components of enzymes which take part in the thyroid hormone biosynthesis including thyroid peroxidase (TPO). (3) TPO is a membrane-bound glycosylated hemoprotein that plays a role in the biosynthesis of thyroid hormones. This enzyme is required for the oxidation of iodide and responsible for the binding of iodine to tyrosyl residue of thyroglobulin (organification). Thyroxine (T4) is synthesized when two molecules of diiodotyrosine (DIT) undergoes an oxidative condensation. The Triiodothyronine (T3) is synthesized by the coupling of one mono-iodotyrosine and one DIT. The deficiency of iron has been reported to decrease plasma concentrations of T3 and T4 and enhance in vitro hepatic rT3 deiodination, suggestive of the thyroid hormone metabolism via a deactivating pathway.(4) It is likely that a minute fraction of T4 gets converted to T3 and a larger percentage is metabolized to a physiologically inactive metabolite, rT3. However, the effect of iron deficiency on deiodinase activity was not clear. (5) Thyroid hormone (T3) plays a vital role in differentiation, development, and maintenance of body homeostasis. The actions of T3 are mediated through intracellular T3-receptor proteins (TRs), which act primarily to modulate transcription by binding to specific T3-response elements in target genes. T3 also exerts important effects at the post-transcriptional level to regulate the expression of several genes. Ferritin is an iron storage protein found in almost all the body tissues involved in iron sequestration with some antioxidant properties. The assessment of serum ferritin, iron and total iron binding capacity (TIBC), which measures percent saturation of transport form transferrin with iron, may be of great significance in hypothyroidism. (6) Keeping these things in mind, the present study was conducted with the aim to estimate and compare the serum ferritin levels in patients with hypothyroidism and healthy controls.

MATERIALS AND METHODS

The present study was conducted in the department of Biochemistry, Superspecialty hospital, Jammu, in which 50 newly diagnosed hypothyroid patients and 50 apparently healthy controls in the age range of 20 years and above of either sex was taken. The diagnosis was based on detailed history and thyroid profile analysis. 5 ml of blood was taken from the antecubital vein under all aseptic conditions and the serum was analyzed for ferritin, thyroid-stimulating hormone (TSH), free and total T3 and T4. Serum total T3, T4 and TSH levels was estimated by sandwich immunoassay using by direct chemiluminiscent technology,(7) Serum FT3 and FT4 were estimated by competitive immunoassay using direct chemiluminiscent technology. (8) The ferritin levels were estimated in abbott architect chemiluminescent microparticle immunoassay.[9] Pregnant or lactating females and those with any associated chronic medical condition or on drugs/ supplements which may affect iron metabolism were excluded from the study.

RESULTS

The study was conducted in 50 healthy controls (comprising of 19 women and 31 men) and 50 type 2 diabetic patients (27 females and 23 males). The mean age of hypothyroid patients was 46.29±8.54 years and the mean age of control group was 41.66±9.69 years. It was observed that there was significant difference in the thyroid profile both total and free. The serum ferritin levels were significantly lower in hypothyroid patients as compared to apparently healthy controls.

Table 1: Comparison of thyroid profile and serum ferritin levels in hypothyroid patients and healthy controls

	Controls	Hypothyroid Patients	p value
Serum Ferritin (ng/ml)	77.98 ±1 6.65	34.08 ± 8.89	<0.0001
Total T3 (ng/ml)	114.26 ± 10.66	84.67 ± 7.78	<0.0001
Total T4 (µg/dl)	9.86 ± 1.79	6.77± 0.97	<0.0001
TSH(µIU/ml)	2.99 ± 1.43	10.86 ± 1.96	<0.0001
FT3 (pg/ml)	2.94 ± 1.01	1.08 ± 0.76	<0.0001
FT4 (ng/ml)	1.59 ± 0.30	0.64 ± 0.24	<0.0001
*p value < 0.05 considered significant			

DISCUSSION

It has been observed that the hypothyroid patients have decreased serum ferritin levels as compared to normal healthy controls. Similar observations were recorded by various researchers. (6,10,11) The presence of hypothyroidism causes decrease gut absorption of iron, leading to its decreased levels, as a consequence of reduced levels of digestive acids/ enzymes or due to associated autoimmune conditions like celiac disease. (12) It may also be as a result of heavy menstruation seen in some female patients. (13) In various studies it has been reported that there is an association between T3 levels and ferritin expression. Besides that the administration of T3 in hypothyroid patients causes a significant rise in the serum ferritin level. The link between T3 and the regulation of ferritin expression suggested that a positive correlation exists between the serum ferritin and T4/T3 levels. (6)

It has also been reported that the iron regulatory protein (IRP, formerly known as the iron-responsive element-binding protein, IREBP, and iron-responsive factor, IRF) is a transacting RNA-binding protein that binds to conserved stem-loop structures, iron-responsive elements (IREs), present in the ferritin, and transferrin receptor (TfR) with high affinity. The IRP also plays a key role in the regulation of homeostasis of iron (14) and binds to the IRE in the 5 -untranslated region (5 -UTR) of ferritin and represses its translation, when there is absence of iron.(15) The binding of the IRP to IREs in the 3 -untranslated region (3 -UTR) of TfR mRNA stabilizes and prevents its degradation of mRNA.(16) When sufficient amount of iron is present, the reverse holds, resulting in increased ferritin translation and decreased TfR mRNA stability. This mutual regulation is accomplished at the post-translational level and is not dependent on new protein synthesis.(17)

Iron forms an important part of the transport mechanism of thyroid hormone into the cells and lack of it can lead to pooling of thyroid hormone leading to metabolically hypothyroid state even in presence of normal FT3 levels. (11) Metal ions, specifically iron, are necessary for the production of extremely reactive hydroxy radicals shifting the balance of body towards increased oxidative stress leading to hypothyroidism. (18) The high TSH level is known to stimulate inflammatory cytokines and reduce the concentration of antioxidants in the body. (19) This may be a supplementary cause for diminished ferritin levels, which possesses antioxidant properties. The T3 hormone also induces gene expression for ferritin.(20) The administration of thyroxine has been reported to increase erythropoietin levels and improve erythropoiesis, thus leading to increased requirement of iron.(21) In hypothyroidism, lack of stimulation of erythroid colony development by thyroid hormones, reduction in the distribution of oxygen to tissues and diminution of erythropoietin level in deficiency leads to anemia and an essential effect on iron metabolism. (22) Hence, it becomes a vicious cycle as deficiency of iron may both be a cause and an effect of hypothyroidism. Thus, hypothyroidism and iron deficiency states are strongly interrelated.

CONCLUSION

Thus, it was observed in our study that there was significant decrease in serum ferritin levels in hypothyroid patients as compared to normal healthy controls that could be a manifestation of disturbed activities of iron-dependent enzymes, which impairs thyroid hormone metabolism. Thus, serum ferritin estimation could be useful for the assessment of thyroid hormone action on the peripheral tissues. Future studies should be done to measure serum ferritin levels before and after thyroid hormone therapy, may endow with valuable information in the diagnosis of thyroid disease.

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