Micronutrient Deficiency in Patients with Hypothyroidism

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Zinc is essential for many biochemical processes and also for cell proliferation. Thyroid hormones influence zinc metabolism by affecting zinc absorption and excretion. Again, zinc deficiency affects thyroid function. It has been suggested that there is an association between thyroid profile and ferritin levels, which is the storage protein for iron in the body. Micronutrients such as serum ferritin and zinc deficiency are associated with hypothyroidism. It has been suggested that there is an association between thyroid profile and ferritin levels, which is the storage protein for iron in the body. This study was undertaken to assess ferritin levels in hypothyroid patients and to observe serum zinc levels in patients with hypothyroidism. This is a cross-sectional study which was carried out in the Department of Biochemistry, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka from July 2014 to June 2015. Here we evaluated 50 subjects (25 normal healthy control, and 25 hypothyroid patients) who were not under medical treatment and did not have previous thyroid surgery or radio-iodine treatment. They were collected from the out-patient department of different tertiary hospitals. The age range of the patients was 20 to 50 years. Thyroid function tests were performed by the chemiluminescence method and trace element such as serum ferritin was measured by kinetic method and serum zinc was measured by spectrophotometer**.** For statistical analysis independent sample "t" test was performed by computer based software SPSS-17.0 version for windows. Serum ferritin and zinc were highly significantly decreased ($p<0.001$) in patients with hypothyroidism. Micronutrient deficiency may be one of the risk factor of the hypothyroidism. Therefore, early detection and supplementation to treat this deficiency may reduce the incidence of hypothyroidism.

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Introduction

Several minerals and trace elements such as iodine, iron, selenium, and zinc are essential for normal thyroid hormone metabolism. Iodine has an important role in the synthesis of thyroid hormones; selenium is a component of the deiodinase enzymes that convert T_4 to T_3. It also protects the thyroid gland from damage by excessive iodide exposure. Zinc appears to be involved in thyroid conversion. Low iron, or more specifically, low ferritin, is one of the most overlooked causes of low thyroid function.[1]

Zinc is involved in T_3 binding to its nuclear receptor and participates in the formation and mechanism of action of TRH. Thyroid hormone binding transcription factors also contain zinc bound to cysteine residues.[2]

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Several groups have documented an association between T_3 levels and ferritin expression. Furthermore, administration of T_3 to hypothyroid individuals produced a significant increase in the serum ferritin level.[1] Although the cause of the T_3-induced increase in the serum ferritin level in humans is unknown; increased synthesis of ferritin in the liver may well be an important contributor. These links between T_3 and the regulation of ferritin expression suggest that a positive correlation exists between the levels of T_4/T_3 and ferritin in the serum. Thus, it has been suggested that serum ferritin measurement could be useful for the evaluation of thyroid hormone action on peripheral tissues.[3]
Plasma ferritin is a measure of iron stores and the best single test to confirm iron deficiency. Low hemoglobin concentration is most readily available sign of anemia, but a significant fall in circulating hemoglobin can not be detected until the final stage of iron deficiency.[4]

Iron deficiency lowers thyroid peroxidase (TPO) activity. TPO is an iron-containing enzyme that initiates the first two steps in thyroid hormone synthesis.[5]

One study has reported sideropenia to be a common finding in women with subclinical hypothyroidism and suggests routinely determining ferritin levels in such patients.[6]
Zinc has important roles in thyroid metabolism.[7] Zinc is involved in T_3 binding to its nuclear receptor and participates in the formation and mechanism of action of TRH. Thyroid hormone binding transcription factors also contain zinc bound to cysteine residues.[8]

Zn is very important in thyrotropin releasing hormone synthesis and is also essential for T_4 to T_3 conversion. It is required for the biological functioning of the thyroid hormones and related receptors. Zn deficiency has a suppressing effect on thyroid hormones, whereas zinc supplementation has an opposite effect.[9]

Our study was designed to see the status of thyroid hormone in patients with low ferritin and zinc level. Iron deficient patients were diagnosed by serum ferritin level <12 µg/L irrespective of age and sex. Iron and zinc deficiency anemia is an advanced stage of iron depletion. Complete treatment of these micronutrient deficiency anemia will decrease the prevalence of iron deficiency and also decrease the burden of hypothyroidism from society.[3]

Methods
The present cross-sectional analytical study was carried out in the department of Biochemistry, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka from July 2014 to June 2015. The study protocol was approved by the Ethical Committee. A total subjects of 50 who were not under medical treatment and did not have previous thyroid surgery or radio-iodine treatment were included in this study. Study subjects were divided into two groups. There were 25 normal healthy control subjects in group A and 25 hypothyroid patients in group B. The age range of the patients was from 20 to 50 years. Anybody having obvious infection, hemolytic anemias; iron-deficiency anemia or severe anemia requiring urgent intervention; cardiac ischemia, gastrointestinal or genitourinary losses due to malignancy and/or acute/subacute blood losses from the respiratory, gastrointestinal, or genitourinary system; pregnancy, hepatic disorder, renal diseases, and polycystic ovarian syndrome were excluded from the study. After selection of subjects, the objectives and the procedures of the study were explained in detail to the subjects. They were informed about the risk and benefit before enrollment of the study. Written, informed consent was obtained from

all patients. Detailed family history and medical history were taken. Ten (10) ml of venous blood was collected from antecubital vein from each subject under all aseptic precaution by disposable syringe. Tests for determination of free T_4, free T_3, TSH and trace elements ie serum zinc and ferritin were carried out as early as possible. Thyroid function tests were performed by the chemiluminescence method and serum ferritin was determined by kinetic method and serum zinc was measured by spectrophotometer**.**

All data were recorded systematically in a preformed sheet and all statistical analysis was done with independent sample "t" test by computer using the software SPSS 17.0 version for windows. Statistical significance was set at $p < 0.05$. All these parameters were compared with age and sex-matched healthy controls.

Data were expressed as mean ±SD.

Results

Mean serum FT_4 level was lower in hypothyroid patients (4.44 ± 3.45) than in control subjects (17.52 ± 2.51) which was statistically significant ($p<0.001$). Mean serum FT_3 level was also lower in hypothyroid patients (2.90 ± 1.68) than in control subjects (4.85 ± 1.04) which was statistically significant ($p<0.001$). Mean serum TSH level was higher in hypothyroid patients (45.72 ± 23.69) than in control subjects (1.65 ± 0.903) with statistically significant difference ($p<0.001$). Serum ferritin was highly significantly decreased ($P<0.0001$) in hypothyroid patients in group B and serum zinc level were also decreased in hypothyroid patients in group B.

Table I: Showing serum ferritin level in two groups

Group	Serum ferritin level Mean ± SD ng/ml Range (L - H) ng/ml	p
A (control) n= 25	4.8656 ± 2.3593 (54 - 105)	<0.0001[HS]
B (case) n= 25	82.2800 ± 11.9566 (2.24 – 9.54)	

n= Number of subjects.
SD= Standard deviation.
t= Unpaired 't' test.
[HS]= Highly significant.
L= Lowest value.
H= Highest value.
#= Normal range of serum ferritin level is 10-120 ng/ml in female and 20-300 ng/ml in male.

Table lI: Showing serum zinc level in two groups

Group	Serum zinc level Mean ± SD ppb/ µgm/l Range (L - H) ppb/µgm/l	p
A (control) n= 25	807.04 ± 156.37 (500 - 1100)	<0.0001[HS]
B (case) n= 25	81.96 ± 13.32 (50 - 100)	

n= Number of subjects.
SD= Standard Deviation.
t= Unpaired 't' test.
[HS]= Highly significant.
L= Lowest value.
H= Highest value.
#= Normal range of serum zinc level is 700 to 1200 ppb/µgm/L.

Discussion

The significant decrease in the level of zinc in hypothyroidism patients are observed as in other different researches. Buchinger et al[10] observed that one of possible explanation for this finding, that gastrointestinal absorption of zinc is severely impaired in hypothyroidism subjects. Yoshida et al[11] found that low zinc level may reflect sequestration of zinc by liver or other tissues. Bellisola et al[12] observed that it is due to the significant influence of TSH in the variation of the concentration of human thyroid tissues.

We have measured the serum FT_3, FT_4 and TSH level in iron deficient patients having low serum ferritin level and in healthy controls. It is observed in this study that the serum FT_4 level was significantly lowered in cases than that of controls ($p<0.001$). This study is consistent with Beard, Borel and Derr.[13] They showed that free T_4 concentrations were significantly lower in iron deficient anemia than normal healthy person and correction of anemia with iron supplementation increases free T_4 levels. Our study also consistent with Etekhari, Keshavarz and Jalali et al.[14] They showed that depletion of iron stores may decrease serum free T_4 level.

In a German epidemiologic study in which 5932 clinically healthy, subjects were tested to evaluate iodine status and goitre prevalence, a significant negative relationship was detected between thyroid volume and zinc levels in subjects older than 40 years, although in other age groups there was no correlation between thyroid volume, iodine status and serum zinc levels.[15]

S Akhter et al[3] suggested that the significant difference in thyroid hormone status in iron deficient people could be a reflection of disturbed activities of iron depended enzymes such as thyroid peroxidase that impairs thyroid hormone metabolism.

Conclusion

From the above discussion, it may be concluded that the reality that most people with hypothyroidism have digestive insufficiency, especially low gastric acid secretion. Gastric acid is essential for the uptake of minerals such as iron and zinc. It stands to reason that low thyroid activity may alter nutrient absorption that may cause iron and zinc deficiency.

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