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ASSESSMENT OF SELENIUM, COPPER AND ZINC IN HYPOTHYROID CASES

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Background: Hypothyroidism is a condition characterized by abnormally low thyroid hormone production. Because thyroid hormone affects growth, development, and many cellular processes, inadequate thyroid hormone has widespread consequences for the body. Hypothyroidism is more common than reported. It is an endemic disease in the northern part of our country. The causes for hypothyroidism in this region are not very clear. Therefore, the role of trace elements in hypothyroidism has been taken up in this study to find if there is any association or not.

Methods: This prospective randomized study consisted of 50 cases in the hypothyroid group that was matched with 26 controls in normal thyroid group. Biochemical parameters such Thyroid Stimulating Hormone, Levothyroxine, Liothyronine, Protein, albumin, globulin, Copper, Zinc, Selenium and Alkaline Phosphatase were determined.

Results: The range level of Copper and selenium was found to be similar and within normal limits among cases and controls of this region. The level of Zinc was lower in cases as compare to controls in females of less than 50 years age group of this region. The levels of total serum Alkaline phosphatase , total protein, albumin and globulin and A/G ratio were within the normal limits among cases and controls of this geographical region.

Key Words: Hypothyroidism, Zinc, Copper, Selenium.

Introduction

Hypothyroidism is a common disorder that occurs when the thyroid gland is underactive and does not produce enough thyroid hormone. A lack of thyroid hormone results in a slowing of the body's chemical processes and metabolism. Hypothyroidism may also lead to serious, potentially life-threatening complications [1].

The thyroid gland secretes two hormones, thyroxine (3,5,3',5' L-tetraiodothyronine) and triiodothyronine (3,5,3'-L triiodothyronine) which are commonly known as T4 and T3 . Their secretion is under the influence of TSH (Thyroid stimulating hormone, also known as thyrotropin) secreted from anterior pituitary gland. The biosynthesis of thyroid hormones involves the trapping of circulating

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iodide by thyroid gland, the incorporation of iodine into tyrosine and the coupling of iodinated tyrosyl residue to form the thyronines (T4 and T3) with the protein backbone of thyroglobulin protein in follicular lumen. Endocytosis followed by proteolytic cleavage of thyroglobulin releases the iodothyronines into the circulation.

Hypothyroidism is a common disease throughout the world. The intensity of the problem is intensified by the multitude of cases remaining undiagnosed due to the problem being subclinical. The incidence of subclinical hypothyroidism increases with age. Hypothyroidism is more common in women than in men. Upto 10% of women over the age of 60 years have subclinical hypothyroidism [1]. In areas with high iodine intake, the incidence of hypothyroidism can be higher than in areas with normal or low iodine intake.

Trace elements serve a variety of functions including catalytic, structural and regulatory activities in which they interact with macromolecules such as enzymes, pro-hormones, presecretary granules and biological membranes. These micronutrients are involved, therefore, in all major metabolic pathways at levels which are so fundamental that the features of deficiency of many of them are variable and non-specific.

Zinc is an integral component of many metalloenzymes in the body; it is involved in the synthesis and stabilization of proteins, DNA, and RNA and plays a structural role in ribosomes and membranes. Since most of the actions of thyroid hormones are mediated by flow of informations through this central dogma, zinc becomes a very crucial mediator for the actions of the hormone. Zinc might be one of the factors in thyroxine to tri-iodothyronine conversion in liver tissue normally [13]. There occurs marked alterations in zinc homoeostasis in thyroid diseases [14].

Copper is necessary for proper iodine metabolism and consequently of proper thyroid hormone synthesis [2].Besides one study indicates that copper controls the DNA encoding of the thyroid hormone receptor.[3]

Deiodinases are enzymes that extract electrons from iodides, and iodides from iodothyronines; so, they are involved in thyroid-hormone regulation, participating in the protection of thyrocytes from damage by H_2O_2 produced for thyroid-hormone biosynthesis [4]. All three deiodinase isoenzymes constituted the family of eukaryotic selenoproteins with identified enzyme functions. Apart from these we further undertook to study the level of Alkaline Phosphatase and protein in our patients. In an experimental study it was found that low-protein diet changes thyroid function in lactating rats [5].

The present study was undertaken to study and find association of above mentioned biochemical parameters with hypothyroidism which might be of use in diagnosis and especially prognosis so that better outcome can be achieved with minimal investigations and better patient response can also be achieved.

Material and Methods

The study was conducted in the Department of Biochemistry and Department of Endocrinology and Metabolism, Institute of Medical Sciences, and in the Department of Botany and Chemical Engineering, Institute of Technology, Banaras Hindu University, Varanasi. Patients coming to the Endocrinology OPD that were already diagnosed cases of hypothyroidism were included in the study with their informed consent as cases. Their age range was between 12 to 55 years, 42females and 8 males. Controls were the patients who visited endocrinology OPD for problems unrelated to thyroid. Their age range was 19 to 60 years and amongst them were 21 females and4 males. The number of cases was 50 and number of controls was 25.

About five milliliters of venous blood from fasting subjects were drawn by utilizing disposable plastic syringes in the morning and transferred into sterile test tube. The blood was allowed to clot and centrifuged at 5000rpm for 10minutes. Sera were separated and stored at -20°C until analysis. Hemolysed samples were discarded.

TSH was estimated by Immunoradiometric assay using IRMAK-9 kit and gamma counter. T4and T3 were estimated by Radioimmunoassay. Alkaline phosphatase, total protein and albumin were measured by colorimetric methods. Zinc, copper and selenium were estimated by atomic absorption spectrophotometry.

Results

As shown in table-1, statistically significant increase in the level of TSH and lowering of T4 were noticed in the cases in comparison to controls. Low values of T3 were noticed in cases which were not significant. The serum values of protein, albumin, globulin and alkaline phosphatase were found to be on the higher side in control group in comparison to the cases. Zinc, copper and selenium all are found to be lower in cases than in the controls though only zinc is found to be statistically lowered.

Discussion

Copper in Hypothyroidism

Copper-deficient and hypothyroid states are considerably enhanced when the 2 existed concurrently, giving added meaning and necessity to close surveillance of trace mineral concentrations and thyroid gland status. In a study on rats there is evidence that copper is necessary for proper iodine metabolism and consequently of proper thyroid hormone synthesis [20]. Copper plays an important role in thyroid metabolism, especially in hormone production and absorption. Copper stimulates the production of the thyroxine hormone (T4), and prevents over-absorption of T4 in the blood cells by controlling the body's calcium levels (Calcium is required for the stabilization of cell membranes and reduces cell permeability).Besides this, copper is also required for the synthesis of phospholipids, that are required for the stimulation of TSH. Therefore correct levels are needed to prevent thyroid problems, and can be used in the treatment of thyroid disease. According to the present study, the serum level of copper in cases was lower than the controls groups. This was in accordance with study by K Aihara, Y Nishi et al 1984 [6].

Zinc in Hypothyroidism

In present study we found significantly low serum level of Zinc in hypothyroid cases compared to our control population. A possible explanation for low zinc level could be high phytate content of Indian diet which mainly consists of high fiber content, cereals and low animal protein. Phytate is known to inhibit zinc absorption [7]. It would have been interesting to note the food habits of our case and control group. Moreover hypothyroid state itself interferes with zinc absorption [8]. So there might be an interesting relationship between hypothyroidism and hypozincemia wherein both might be reinforcing each other leading to a vicious cycle.

Selenium in Hypothyroidism

Selenocysteine is found in the deiodinase enzymes, which mediate the deiodination of thyroxine to triiodothyronine. The importance of selenium for thyroid hormone metabolism [9,10,11] is evident from changes in the T3-T4 ratio which develop after relatively mild selenium depletion in infants and elderly (65+ years) subjects. Communities noted for a high incidence of myxedematous cretinism have been found to have low plasma selenium status and GSHPx activity in addition to having low iodine status [12] and being exposed to high thiocyanate intakes from cassava.

Total protein in hypothyroidism

The sterol hormone binding proteins (SHBP) also bind thyroid hormone (TH. Both thyroid hormones circulate in blood bound to plasma proteins; only 0.04% of T4 and 0.4% of T3 are unbound or free, and consequently, available for entry and action in target tissues. There are three major thyroid hormone transport proteins: thyroxine-binding globulin (TBG); transthyretin, formerly called thyroxine-binding prealbumin (TBPA), and albumin. According to the present study, their was no significant difference found in serum level of total protein between cases and controls groups though low levels have been reported.

Albumin in hypothyroidism

Albumin has one strong binding site for T4 and T3 and several weaker ones. Because of its high concentration in serum, albumin carries about 15% of circulating T4 and T3. The rapid dissociation rates of T4 and T3 from albumin make this carrier a major source of free hormone to tissues. Hypoalbuminemia, as occurs in nephrosis or in cirrhosisof the liver, is associated with a low total T4 and T3, but the free hormone levels are normal.

Alkaline Phosphatase in Hypothyroidism

According to the present study, their was no significant difference found in serum level of alkaline phosphatase between cases and controls groups. In a study, hyperthyroid patients have shown higher levels of alkaline phosphatase (ALP) and osteocalcin, and a higher urinary deoxypyridinoline/creatinine ratio, compared with controls ($P<.05$). In subclinical hyperthyroidism, only ALP was found to be higher compared with control values. Not many studies have been done on this topic. There were reports of lowered alkaline phosphate inpatients of cretinism, while another study indicated insignificant rise in the alkaline phosphate in hypothyroid patients. Similar findings have been observed in our study also.

Conclusion

From the results obtained from the study, it is clear that the level of Copper, Selenium and of Zinc were lower in cases as compared to controls. The levels of total serum protein, albumin and globulin and Alkaline phosphatase were lower among cases and controls of this geographical region but no significant difference was found between cases and controls. To conclude, the present study gives us an idea that the deficiency in trace elements like zinc, copper and selenium might be one of the causes of hypothyroidism. However, since the size of study group was very small, it needs to be studied further with groups.

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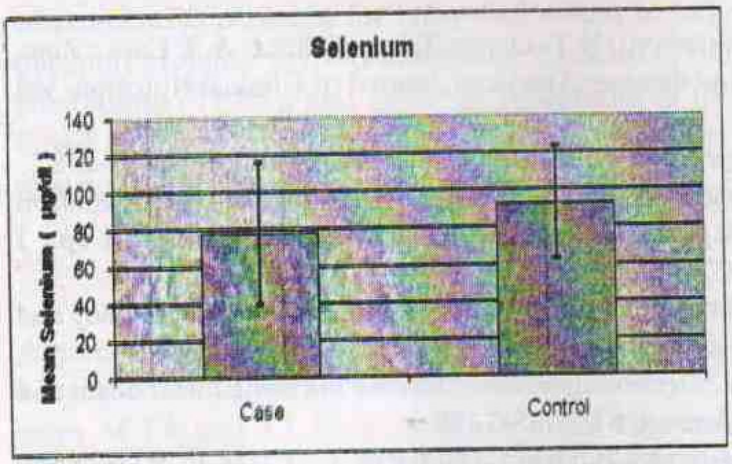
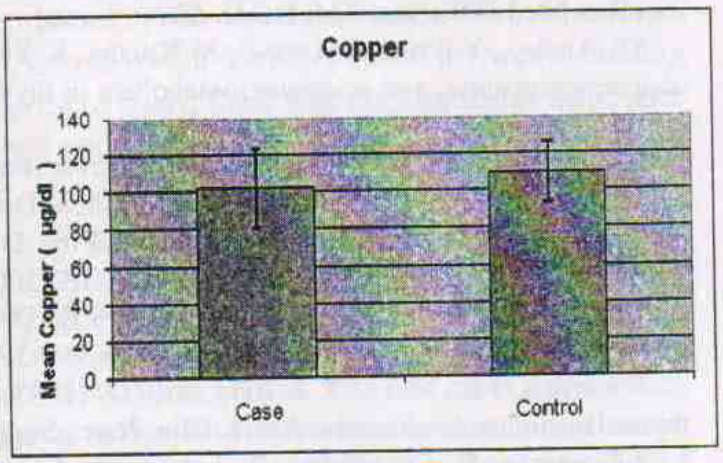
TABLE 1

Parameters	Cases	Control	P-Value	Significance
Serum T3 (µgm/dl)	92.98±18.44	98.00±18.84	0.279	Not significant

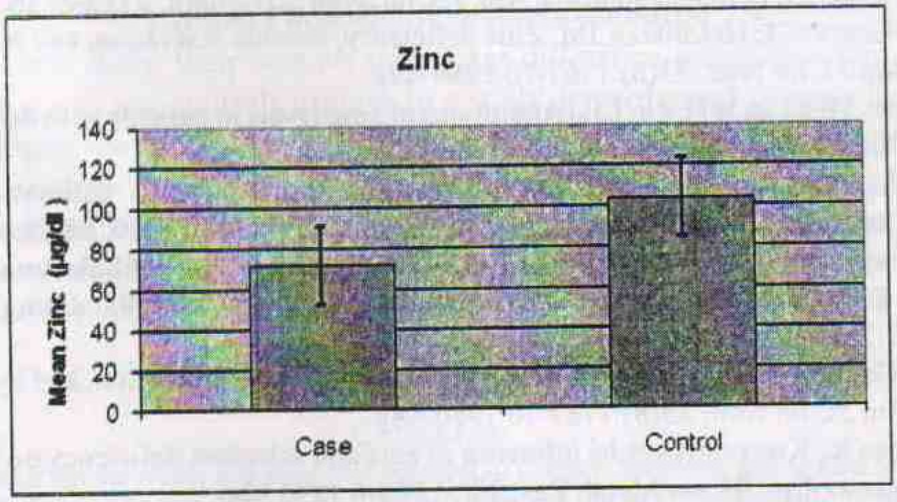
Serum T4 (µgm/dl)	5.50±1.63	9.48±1.66	<0.001	Significant
Serum TSH (IU/L)	16.47±17.08	1.24±.920	<0.001	Significant
Serum protein (gm/dl)	6.22±1.37	6.74±1.72	0.200	Not significant
Serum Albumin (gm/dl)	3.59±.86	3.91±.78	0.117	Not significant
Serum globulin (gm/dl)	2.61±.65	2.83±1.08	0.354	Not significant
Alkaline PO4 (KU/dl)	7.77±3.77	8.03±5.9	0.840	Not significant
Serum copper (µgm/dl)	102.05±21.12	109.6±16.52	0.095	Not significant
Serum zinc (µgm/dl)	72.10±19.51	103.9±19.09	<0.001	Significant
Serum Selenium (µgm/dl)	77.96±38.1	92.72±30.12	0.073	Not significant



Graph showing the mean and standard deviation of serum selenium in cases and controls



Graph showing the mean and standard deviation of serum copper in cases and controls



Graph showing the mean and standard deviation of serum zinc in cases and controls