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Comparative Study of Trace Elements in Healthy Controls and Hypothyroidism Patients in Western Rajasthan

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ABSTRACT

The association of serum trace elements like selenium, zinc, manganese and copper has been found in patients with thyroid dysfunctions. This study was conducted to see the serum level of these four trace elements in hypothyroid patients and serum levels of free T3, T4 and TSH detection by chemilumminisence method of confirmed 95 hypothyroid patients (28 males, 67 females), and results was compared with age and sex matched 95 healthy subjects were included in this study. Both control and study group patients were of same socio-economic status and dietary habits. Serum levels of zinc, manganese and copper were estimated using standard absorption spectrophotometer technique and serum level of selenium by hydride generation method. We observed significant low serum levels of zinc, copper and selenium, while high level of serum manganese in hypothyroidism patients, as compared with normal healthy controls. The result showed a significant association of trace elements with hypothyroidism.

KEYWORDS : Hypothyroidism, Trace elements, Atomic absorption spectrophotometer.

INTRODUCTION

The burden of thyroid disease in the general population is enormous. Thyroid disorders are the most common among all the endocrine diseases in India. [1]

The importance of the thyroid gland in maintaining human health is well recognized. Since iodine is a crucial constituent of thyroid hormones, it is not surprising that thyroid dysfunction is very common in geographical areas of iodine deficiency. However, even when this trace element is present in adequate supply, thyroid disease is present in 3-5% of the population. [2] In India thyroid disorders are in a transition zone from a predominant iodine deficient nation to now an iodine sufficient population. [3]

According to a projection from various studies on thyroid disease, it has been estimated that about 42 million people in India suffer from thyroid diseases. [4] The true prevalence and incidence in India of thyroid disorders is difficult to estimate, functional studies of the goitrous subjects showed overall prevalence of 5.4% hypothyroidism, 1.9% hyperthyroidism. 7.5% prevalence of autoimmune thyroiditis was demonstrable by fine needle aspiration biopsy among female goitrous students. [5]

The maintenance of optimal health requires an adequate supply of carbohydrates, proteins and lipids, and macronutrients, micronutrients, and trace elements. [6] Trace elements are known to influence hormones at levels of action, including hormone secretion and activity and binding to target tissue. Conversely, hormones influence trace metals metabolism at several levels of action, including excretion and transport of trace metals. [7; 8] Hence, trace elements assay in biological fluids can be used as diagnostic or prognostic aid in patients with different hormonal disturbances alongside with other biochemical parameters.

The status of different trace elements in hypothyroidism is not well established. Furthermore, serum manganese in hypothyroidism patients is not well studied previously. In this work, the serum contents of some trace elements (Se, Zn, Cu, and Mn) were determined in hypothyroidism patients and compared with that of normal subjects.

METHODS

This study was designed to evaluate serum selenium, zinc, copper and manganese levels in serum of 95 patients with hypothyroid disorder (27 males, 68 females). The data obtained from our study is to be compared with age and sex matched 95 normal healthy persons without thyroid disease or any other clinical problems. Both study and control group were of same socio-economic status with similar diet habits.

The patients were diagnosed depending on the results of clinical examinations, serum hormone levels (free T3, T4 and TSH), computed tomography scan, pathological examinations and fine needle aspiration (if needed).

The criteria for the selection of patients were:-

Persons with known hypothyroidism and serum levels of TSH >4.25 mIU/L, free T3 <3.7 pmol/L and free T4 <10.3 pmol/L considered as a hypothyroidism patients.

Age 18-70 years.

Exclusion criteria:- Patient with the following condition:-

1. Age under 18 and above 70 years and who do not given the consent.
2. Gastro intestinal disorder, which affects absorption.
3. Patients with malignancy, pregnancy, any liver disorder, renal disorder or any chronic disease.
4. Patient with any endocrine disorder other than hypothyroidism that directly or indirectly affect trace element levels.
5. Drugs affecting levels of trace elements, which were not taking during last 10 days.
6. Have any thyroid surgery in past.

Sample collection and Preparation:- Taking written consent from all the subjects before taking the samples. About 10 ml of blood was drawn from the ante-cubital vein by aseptic techniques and transferred to a well cleaned and metal free test tube without any anticoagulant to avoid hemolysis. The plain test tube was left at room temperature for 20 minutes and after clotting, centrifuged at 2500 rpm for 15 minutes. Half amount of serum was transferred to another metal free test tube by using a well cleaned auto pipettes and was stored at -20ºC after proper labeling and securely packed for measuring trace elements by Atomic Absorption Spectroscopy (AAS) in different batches.

The remaining amount of serum was sent to Immune assay lab same

day for the evaluation of free T3, T4 and TSH levels by chemilumminisence immune assay (modal Elecsys 2010 of Roche HITACHI), which is a fully autoanalyzer.

The zinc, copper, and manganese levels in the serum of each subject were measured with the help of flame atomic absorption spectroscopy (AAS SHIMADZU, modal AA-7000) under standard set protocol. The determination of selenium concentration was done by hydride generation method. Serum was digested by a mixture of nitric and perchloric acid. After hydride generation and using a sodium borohydride method, the selenium concentration was determined by AAS. Analytical reagent grade chemicals and standards were used. Distilled water used for washing laboratory apparatus and for preparing solutions and standards.

RESULTS

In this study, the results as presented in the table 1 and figure 1a & 1b, shows that the levels of trace element were altered in subjects having hypothyroid disorder and results of study were expressed as mean **± standard deviation.**

The levels of selenium, zinc and copper in the serum of hypothyroidism patients were significantly decreased (P<0.001) than the levels in normal healthy controls as shown in the table 1 and figure 1a.

While the level of manganese in serum of hypothyroidism patients were significantly increased (P<0.001) than the level in normal healthy controls as shown in the table 1 and figure 1b.

DISCUSSION

The findings of the present study indicates that majority of our patients were women and in the age group of 31 to 40 years. The female hypothyroid patients constituted about 71.57% of the total.

Table 1: Mean + SD of various trace elements of case & control group subjects.

Trace Element	Mean ± SD		P-value
	Hypothyroid Cases	Normal Healthy Controls	
Selenium (Se) µg/l	53.66 ± 10.31	114.35 ± 22.5	<0.001
Zinc (Zn) µg/dl	67.19 ± 9.51	103.06 ±10.29	<0.001
Copper (Cu) µg/dl	75.62 ±10.70	118.52 ±17.29	<0.001
Manganese (Mn) µg/l	1.69 ± 0.42	0.92 ± 0.19	<0.001

Figure 1a: Graph showing the mean of various trace elements Cu, Zn and Se of case & control group subjects.

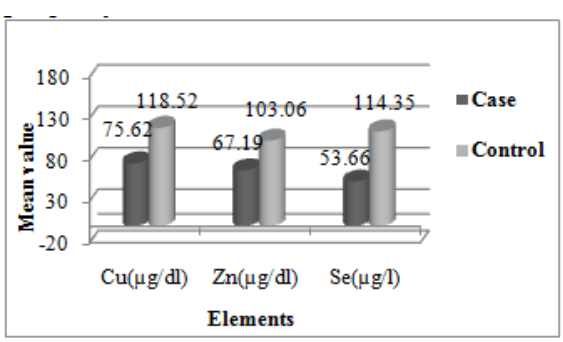
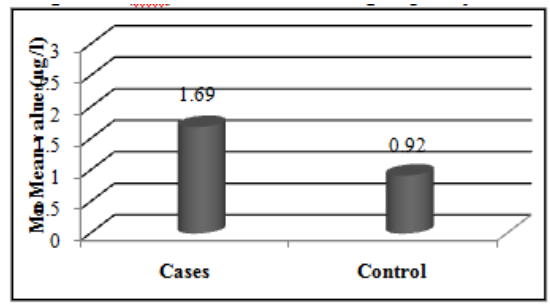


Figure 1b: Graph showing mean of trace element manganese (Mn) of case & control group subjects.



Earlier statistics also have suggested that hypothyroidism is six times more common in women than in men. The higher prevalence of thyroid disease in women suggests that estrogen might be involved in the pathophysiology of thyroid dysfunction. Estradiol has an antagonistic effect on the hormones T3 and T4. The reason being, estradiol competes with T3 and T4 for binding sites on the receptor proteins. [9]

Our study also indicates a strong association of Se, Zn, Cu and Mn with hypothyroidism. In hypothyroid patients there were significantly lower serum levels of Zn, Cu and Se as compared to controls, this correlates with the study of Ambooken Betsy et al. (2013). [10]

The decrease in serum selenium levels in hypothyroidism patients was in agreement with the studies of other researcher such as Erdal et al. (2008), indicating the important role of selenium in controlling the thyroid gland functions.[11] These findings were also supported by the study of Anne Drutel et al (2013). [12] Arthur J.R. (1996) and Chanoine J.P. (2001) extracted that one possible explanation for these findings, the iodothyronine 5'-deiodinases, which is responsible for the conversion of thyroxine (T4) to its active form triiodothyronine (T3), is selenoenzyme. In conclusion, when selenium is depleted, there is less Se to form the 5'-deiodinase enzymes, resulting in low T3 and hypothyroidism. [13; 14]

Another explanation also showed in the study of Chanoine J.P. (2001) and Neve J. (1995), selenium supplementation caused an increase in plasma selenium values but did not affect the activity of the selenoenzyme glutathione peroxidase (one of the body's prime antioxidants) used as a marker of selenium status and caused a significant decrease in thyroglobulin values due to greater levels of reactive oxygen species and hydrogen peroxide, which lead to increased damage to the thyroid gland. [14; 15]

Similar types of results of zinc were also found in the researches of Zhang et al. (2004) and Abdulkerim Kasim et al. (2013).[16; 17] Yoshida K et al (1990) in his study suggest the one possible explanation for these findings that gastrointestinal absorption of zinc is severely impaired in hypothyroidism subjects. An alternative explanation would be a change in zinc distribution; the low zinc level may reflect sequestration of zinc by the liver or other tissues. [18] Another explanation also observed in the study of Bellisola (1998), is due to the significant influence of TSH in the variation of the concentration of iodine, selenium and zinc in normal and altered human thyroid tissues. [19]

Dhawan et al (2007) and Pekary et al (1991) extracted that zinc has important roles in thyroid metabolism, it involves in T3 binding to its nuclear receptor, and participates in the formation and mechanism of action of TRH. [20;21] Hence, the correlation between hypothyroidism and serum zinc is not a simple correlation and needs more specific studies.

In our study the serum level of copper was found significantly decreased in patients with hypothyroidism as compared with healthy control. Esipenko BE et al. (1990) observe in his study on rats, there is evidence that copper is necessary for proper iodine metabolism and consequently of proper thyroid hormone synthesis. [22] While Abdulkerim Kasim Baltaci et al (2013), assess the Se, Cu and Zn in hypothyroid cases, they showed that patients had lower selenium and zinc levels while higher copper levels. [17] And in the another research of Al-Juboori et al. (2009) found that there was no significant change in serum copper in patients with hypothyroidism as compared to that of normal subjects.[23] There is no precise evidence, in literature, corre-

sponding to the correlation between serum copper and hypothyroidism. More investigations would be required using larger sample size and severe hypothyroidism to be sure about the lack of correlation between the disease and different copper indexes.

Our study showed that serum level of manganese in hypothyroidism patients significantly increase when compared with normal healthy controls. The results are correlated with the findings of Al-Juboori et al (2009), they also showed in his study that increase serum Mn level in hypothyroid patients.[23] Soldin and Aschner M. (2007) hypothesized that manganese may directly or indirectly affect the thyroid function by injuring the thyroid gland or dysregulating dopaminergic modulation of thyroid hormone synthesis. [24] The direct cause for the increase in serum manganese is not understood and there is no direct correlation between serum manganese and hypothyroidism. Previously there was so little evidences, in literature, represent the increase in serum manganese in hypothyroidism patients. More studies would be needed to explain the real cause about the increase in serum manganese in hypothyroidism.

CONCLUSION

To conclude, the present study gives us an idea that abnormal metabolisms of selenium, zinc, manganese, and copper in hypothyroidism disease. Considering all that, the correction of serum trace elements concentration would have a beneficial effect on treatment, complication and progression of the diseases, selenoproteins levels for selenium status, ceruloplasmin for copper status should be detected and patients with hypothyroidism should be screened for atrophic gastritis. More comprehensive study with large samples should required, so it would be recommendable to provide laboratory analysis of trace elements as a routine and also have the scope for further deep research in this field because thyroid disorders are most common among all the endocrine diseases.

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