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STUDY OF HOMOCYSTEINE LEVELS IN OVERT HYPOTHYROID PATIENTS

Biochemistry

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ABSTRACT

Hypothyroidism is the clinical syndrome resulting from deficiency of thyroid hormones. It mainly affects women and is more prevalent in the middle-aged and elderly. In overt hypothyroidism, TSH levels are high and T4 & T3 levels are low. It can also be diagnosed in those who have a TSH on multiple occasions greater than 5mIU/L, appropriate symptoms, and only a borderline low T4. Patients with hypothyroidism are prone to develop cardiovascular disease, which is related to elevated cholesterol and lipoprotein levels in these patients. Serum Homocysteine concentration is also associated with increase in the incidence of cardiovascular diseases. So this study was conducted with the aim to measure serum levels of homocysteine in patients with overt Hypothyroidism and to find out possible relationship between them. In this study 70 cases of overt hypothyroid patients along with 70 healthy subjects (age and gender matched) were enrolled. Thyroid hormones along with Homocysteine levels were assessed. Serum Homocysteine levels were found higher in Overt Hypothyroid subjects ($P<0.0001$) when compared to healthy controls. Study concluded that serum homocysteine is a valuable markers in overt hypothyroid subjects to predict the possibility of development of any cardiovascular complications accompanying Hypothyroidism

KEYWORDS

Homocysteine, Hypothyroidism, Overt Hypothyroidism.

I. INTRODUCTION

Hypothyroidism is a disorder in which thyroid activity is reduced due to which it does not produce enough thyroid hormones. This leads to hyper secretion of pituitary thyroid stimulating hormone (TSH) and an increase in the serum level of TSH. Thyroid hormones, Thyroxine (T4), and Triiodothyronine (T3) play an important role in all major metabolic pathways by regulating protein, carbohydrate, and lipid metabolism; including synthesis, mobilization, and degradation.[1]

Patients with hypothyroidism are prone to develop cardiovascular disease, which is in accordance with autopsy studies showing that the atherosclerotic process is increased in hypothyroidism [2] and decreased in hyperthyroidism. [4] The increased cardiovascular morbidity in hypothyroid patients has been related to elevated cholesterol and lipoprotein levels, which are normalized after thyroid hormones replacement. [3] Thyroid hormones are known to affect the heart and vasculature and as a result the impact of Overt Hypothyroidism on the cardiovascular system has recently become an important topic of research. [4]Increased incidence of cardiovascular diseases in hypothyroidism cannot be fully explained by an atherogenic lipid profile.

Thyroid hormones are physiologic modulators of both tissue oxidative stress and protein degradation. The mechanism linking hypothyroidism and oxidative stress is unknown. Oxidative stress increases the concentration of oxidised Low-Density Lipoprotein (LDL).

Homocysteine is sulphur containing non-protein α-amino acid. It also induces LDL oxidation. Serum total homocysteine level has been recently postulated as an independent risk factor for accelerated atherosclerosis. [5] Abnormally high serum homocysteine level is known as hyperhomocysteinaemia, conventionally described as above 15 µmol/L. Hyperhomocysteinaemia in hypothyroidism may probably be due to reduced renal excretion and reduced metabolism of homocysteine. Meta-analysis of cross-sectional studies has suggested that increased serum Homocysteine concentration is associated with 60 percent increase in the incidence of cardiovascular diseases. [6]

Since Homocysteine is an unstable amino acid, in hyperhomocysteinaemia, it undergoes auto-oxidation and produces reactive oxygen species. These reactive oxygen species, inactivates and deplete nitric oxide and impair endothelial thrombomodulin expression that leads to activation of contact pathway for intrinsic coagulation in endothelial cells. All these factors lead to endothelial damage and dysfunction. [7]

Homocysteine can reflect the severity of coronary artery disease to a certain extent. Hypothyroidism with high Homocysteine predicts a higher prevalence of Cardiovascular Disease, especially atherosclerosis. [8] Secondly, hypothyroidism is closely related to hyperlipidemia. Homocysteine concentration is also associated with hyperlipidemia. Hence, the study tries to find out the relationship between Homocysteine concentration and Overt Hypothyroidsim among the study subjects.

II. MATERIAL & METHOD

This study was conducted on 70 cases of overt hypothyroid patients of both gender and age attending the OPD of Department of Medicine, J.L.N. Medical College & Associated group of Hospitals, Ajmer. The results were compared with age and gender matched 70 subjects acting as controls. Diagnosis of thyroid disorder has been made according to the criteria recommended by the European Thyroid Association Guidelines-2013. Consent from all the subjects was obtained for the study. Blood samples were collected from anticubital vein by venepuncture in plain vials. Serum was separated by centrifugation at 2500 rpm for 10 minutes and stored at - 20^{0}C.

Exclusion criteria-

1. History of renal disease, cerebrovascular or cardiovascular diseases
2. Thyroid supplementation and anti thyroid agents
3. Diabetes Mellitus
4. Chronic Alcoholism
5. Hypertension
6. Pregnancy
7. Positive clinical history of any Malignancy

Serum Free Triiodothyronine (Ft_3), Serum Free Thyroxine (FT_4) and Serum Thyroid Stimulating Hormone (TSH) were measured using Enzyme Linked Immunosorbent Assay (ELISA). Serum Homocysteine was also measured using the Enzyme Linked Immunosorbent Assay (ELISA) technique.

Data was recorded in a predesigned performa, managed in an excel spread sheet and was reported as mean ± SD median (range). Comparison of physical and biochemical parameters between overt hypothyroid subjects and Healthy controls was performed using equal or unequal variance unpaired student t-test for continuous variables (as applicable).

All p-values were based on a two sided test of statistical significance. Significance was accepted at the level of $p<0.05$.

III. RESULTS AND OBSERVATION

In this study, the healthy controls were in GroupI, and overt hypothyroid subjects were in GroupII.

A highly significant ($p<0.0001$) decrease in mean Serum fT3 level was observed in overt hypothyroid subjects (group-II) when compared to control (group I) as shown in Table I. A similar trend was observed in mean Serum fT4 level in group-II when statistically compared to group-I. The mean Serum TSH level was found to be significantly high in overt hypothyroid subjects (2.15±1.09 vs. 34.76±11.92) as compared to healthy controls (Table I).

Fig.1 shows that mean serum Homocysteine level in overt hypothyroid subjects was found to be significantly higher in comparison to healthy subjects i.e. (11.68±2.54 vs. 25.74±4.19).

Table I: Comparision Of Biochemical Parameters In Healthy Control And Overt Hypothyroid Subjects

Parameter	(GroupI) Healthy controls (n=70) Mean±SD	(GroupII) Overt Hypothyroid subjects (n=70) Mean±SD	'P' Value*
fT3 (pg/ml)	3.10±0.42	2.43±0.52	P < 0.0001
fT4 (ng/dl)	1.56±0.38	0.54±0.29	P < 0.0001
TSH (µIU/ml)	2.15±1.09	34.76±11.92	P < 0.0001
Homocysteine (µmol/L)	11.68±2.54	25.74±4.19	P < 0.0001

P value <0.0001 is considered Highly Significant(HS), $p<0.01$ is Significant(S) while $p>0.05$ is Non Significant (NS)

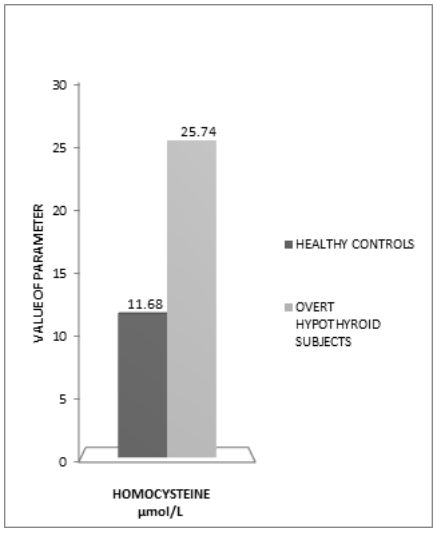

Fig.1 Comparision Of Homocysteine Levels In Healthy Control And Overt Hypothyroid Subjects

IV. DISCUSSION

Many studies have shown that Homocysteine levels are affected in subclinical hypothyroidism .Very few studies have evaluated its levels in overt hypothyroidism The present study was carried out to analyse the role of homocysteine as a predictive marker for cardiovascular diseases in overt hypothyroid cases.

Table-1 shows the biochemical parameters viz, serum fT3 (pg/ml), serum fT4 (ng/dl), serum TSH (µIU/ml) and serum Homocysteine (µmol/L) levels in normal healthy controls and Overt Hypothyroid subjects.

Based on Fig. 1, the mean serum Homocysteine level in hypothyroid subjects (25.74±4.19 µmol/L) was found to be higher than healthy controls (11.68±2.54 µmol/L; P < 0.0001).

Our study is in line with Chandankhede M et al. (2018) who found that Homocysteine levels are raised along with TSH suggesting that in hypothyroidism increased homocysteine may increase the risk for atherogenesis and cardiovascular complications. Thus measuring the Homocysteine along with TSH can help in assessment of cardiovascular status and also maintaining appropriate TSH levels favours improvement of health status in hypothyroid patients.

Bamashmoos SA et al. (2013) also suggested that homocysteine is significantly related to TSH, creatinine and age and negatively related to fT4 and no relations with fT3 and cholesterol. Similar observations have been made in some but not all studies (Orzechowska et al. (2007); Lien et al. (2000) and Nedrebo et al. (1998). The increase observed in homocysteine in these patients may explain and contribute to a higher cardiovascular risk, since an earlier study indicates that an increase in plasma Homocysteine level of 4 µmol/l, confers a 40% increase in relative risk for coronary heart disease compared with healthy controls.

V. CONCLUSION

From the present study it can be concluded that in Overt Hypothyroidism, Homocysteine levels are elevated. Similar observations are seen in Atherogenesis i.e. Hyperhomocysteinemia is found to be associated with atherosclerotic lesions.

Thus in conclusion it can be stated that the severity of hypothyroidism together with hypercholesterolemia, may explain and contribute to atherogenesis. This might have diagnostic significance for the prediction of cardiovascular diseases. Therefore, we recommend screening of serum homocysteine as valuable markers in overt hypothyroid subjects to predict the possibility of development of any cardiovascular complications accompanying Hypothyroidism.

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