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Relation between Homocystine, Creatinine and Cholesterol in Overt Hypothyroidism

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ABSTRACT

INTRODUCTION

Hypothyroidism is a condition which is In serious cases, it is quickly detected and managed, but it can be fatal if left untreated. The description of hypothyroidism is based on statistical reference ranges for the respective biochemical parameters, and it is a hotly debated subject. Medical hypothyroidism can manifest itself in a number of ways, ranging from no symptoms to a life-threatening disease. Overt hypothyroidism is characterised as hypothyroidism with elevated TSH and low T4. The most common symptoms of hypothyroidism in adults are exhaustion, lethargy, cold aversion, weight gain, constipation, voice change, and dry skin, although clinical appearance differs based on age and sex, among other variables.Thyroid hormones can influence cholesterol metabolism, resulting in elevated serum cholesterol. Thyroid hormones may have a direct effect on renal function, tHcy metabolism, and kidney clearance, resulting in an increase in serum creatinine.

AIM: Relation between Homocystine, Creatinine and Cholesterol in Overt Hypothyroidism

MATERIAL AND METHOD: The present study included total 200 subjects that were divided in two groups. Group I contained 100 patients with overt hypothyroidism and Group II containd100 healthy individuals as control group. Blood samples from the subjects were collected and analysed for Serum Homocysteine, Serum Creatinine, Cholesterol and thyroid hormones FT3, FT4 and TSH.

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RESULT: Total Homocysteine, Total Cholesterol, Serum Creatinine and TSH is significantly increased (P<0.0001) in overt hypothyroidism patients when compared them with the healthy individuals, while the patients with overt hypothyroidism had reduced FT3 and FT4 which was statistically significant as compared to control group.

CONCLUSION: Our analysis indicated that increased plasma tHcy, In overt hypothyroidism, total cholesterol and creatinine were found, as well as an inverse relationship between tHcy and FT4 and FT3, as well as a positive relationship with TSH.

ABBREVIATION: Overt Hypothyroidism, Homocysteine,Cholesterol, Creatinine& TSH

INTRODUCTION

According to the degree of thyroid function loss, hypothyroidism is classified into two types: subclinical hypothyroidism (SH) and overt hypothyroidism (OH). [1] A persistently elevated plasma thyroid stimulating hormone (TSH) level in the presence of normal free thyroxin is classified as SH (FT4). [2] Subclinical thyroid failure is often asymptomatic; 30 percent of patients with SH may report symptoms suggesting thyroid hormone deficiency. [3] SH has recently been related to the development of atherosclerosis and myocardial infarction in elderly women. [4]OH is a risk factor for cardiovascular diseases, especially coronary heart disease, as it is characterized by high TSH levels and low levels of FT4 and/or free triiodothyronine (FT3). [5]

Hypothyroidism is related to a higher risk of atherosclerotic cardiovascular disease[6] and cardiovascular morbidity[7], which is consistent with autopsy findings that hypothyroidism accelerates the atherosclerotic phase. [8]Higher levels of cholesterol and low-density lipoprotein cholesterol (LDL-C) have been linked to increased cardiovascular morbidity in hypothyroid patients, who are stabilised after thyroid hormone replacement. [9] Other pathogenic factors may be responsible, as lipid disorders in hypothyroid patients do not fully account for increased atherosclerosis and cardiovascular disease. [10,11]

Epidemiology

Prevalence and risk factors

In the general population, the prevalence of overt hypothyroidism ranges between 0–3 percent and 3–7 percent in the United States, and between 0–2 percent and 5–3 percent in Europe, depending on the term used. The prevalence of undiagnosed hypothyroidism, for both overt and mild cases, was reported to be about 5% in a meta-analysis [13] of studies from nine European countries. Hypothyroidism is more common in populations with a relatively high iodine intake as well as in highly iodine-deficient populations, owing to variations in iodine status.[14]Hypothyroidism is more prevalent in women, the elderly (>65 years), and white people, though evidence on ethnic differences is limited.[15] Hypothyroidism is more common in people that have autoimmune disorders like type 1 diabetes, autoimmune gastric atrophy, or coeliac disease, and it may be a symptom of a number of autoimmune endocrinopathies. Hypothyroidism is more common in people who have Down's syndrome or Turner syndrome.

Plasma complete homocysteine (tHcy) is a recognised risk factor for cardiovascular disease [16]. It has frequently been linked to occlusive vascular disease in the absence of any other recognised risk factors. In the presence of elevated plasma levels of Hcy, platelet aggregation, plasma anticoagulant functions, and vascular vasomotor activity are all affected[17]. Several genetic and acquired factors influence the

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plasma level of tHcy, which is elevated in cases of vitamin folate and Cobalamin deficiency, as well as in renal failure.[18]We compared the levels of serum total homocysteine (tHcy), T.cholesterol, creatinine, and thyroid hormones fT3, fT4, and TSH in diagnosed overt hypothyroid patients to control subjects in this research.

MATERIAL AND METHODS

From December 2019 to July 2020, researchers at Datta Meghe Medical College and Shalinitai Meghe Hospital and Research Centre conducted this research. There were 200 participants in the survey, ranging in age from 20 to 55. The study included 120 newly diagnosed, untreated overt hypothyroid patients (80 females and 40 males) with a mean age of 39.43±7.24 years (ranged from 23 to 55 years). Patients with any heart, kidney, or bone disorder, as well as treated patients and pregnant women, were not included in the report.These patients were chosen at random each day from patients who had been referred to the DMMC and SMHRC outpatient endocrinology and general surgery departments for CLIA thyroid hormone measurements. Low serum fT4 and/or fT3 levels, as well as high TSH levels, were used to diagnose overt hypothyroidism. The control group consisted of 80 average non-hypothyroid volunteers from the DMMC and SMHRC staff (F=40; M=40) (mean age SD, 28.25±6.54; ranged from 20–45 years old). To take part in this study, all participants gave their informed consent.

Sample collection

Patients and controls were given non-fasting blood samples (5ml) of venous blood at random. The serum was isolated and estimated for fT3, fT4, TSH, overall homocysteine, total cholesterol, and creatinine levels after being left to clot for 30 minutes and centrifuged for 5 minutes.

BIOCHEMICAL ANALYSIS [19-24]

Determination of total homocysteine (tHcy)

Complete homocysteine (tHcy) concentrations in the blood were calculated using a enzyme immunoassay (EIA) reagent package. Reference Range of tHcy was 5 and 15 μmol/L .

Total cholesterol and creatinine levels are calculated.

Serum total cholesterol estimation was done by CHOD-PAP method and concentrations of creatinine were calculated by enzymatic method utilizing kits and were run on Fully automatedAnalyzer. The standard level for total cholesterol in the blood (up to 200 mg/dl), creatinine (female; 0.6-1.3mg/dl, male: 0.7-1.5 mg/dl).

Determination of thyroid hormones

TSH estimation was done by CLIA by two-site immunoenzymatic (“sandwich”) assay. The reference range for TSH was 0.34-5.6 μIU/ml. Free T3 estimation was done by CLIA by competitive binding immunoenzymatic assay. The reference range for FT3 was 3.8-6pmol/L Free T4 estimation was done by CLIA by two-step enzyme immunoassay.The reference range for serum FT4was 0.61-1.12 ng/ml.

STATISTICAL ANALYSIS

The data was statistically analysed using SPSS version 20. Calculated values were processed using the arithmetic mean, standard deviation, and Students‘t’ test for quantitative results.P value of < 0.05 was considered as statically significant.

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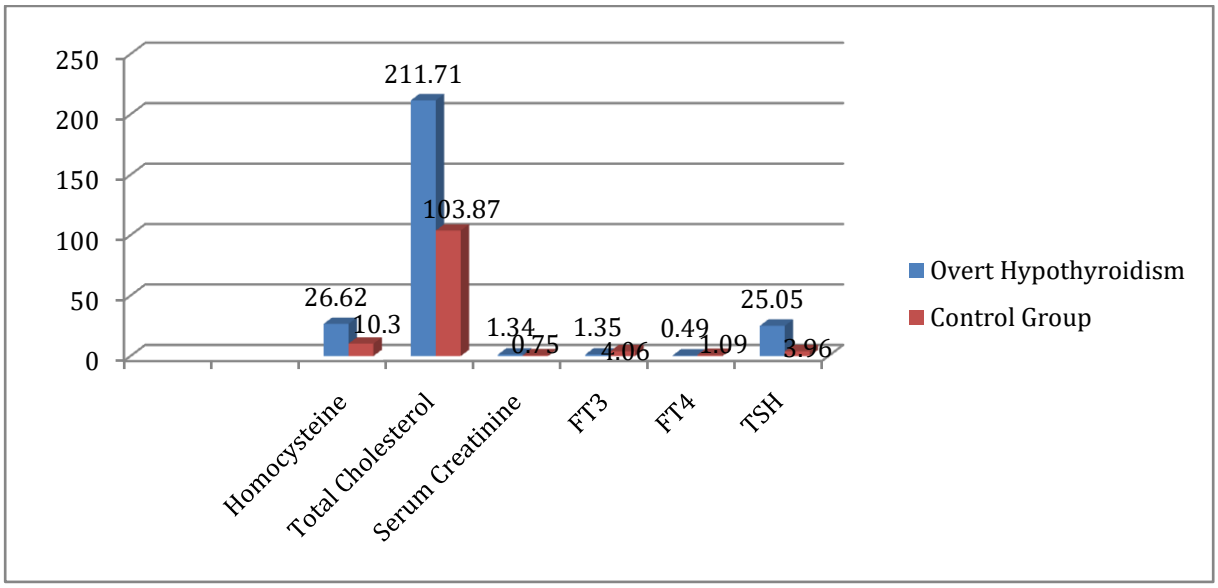
RESULT

Table 1: Comparison between levels of serum Homocysteine, total Cholesterol, Serum Creatinine, Free T3, Free T4 and thyroid stimulating hormone in overt hypothyroidism study and control group

Parameters	**Overt Hypothyroidism N=100 (Mean±SD)**	**Control Group N=100 (Mean±SD)**	**P- Value**
Homocysteine (µmol/L)	26.62 ± 6.14	10.30 ± 3.84	P < 0.0001
Total Cholesterol (mg/dl)	211.71 ± 25.28	103.87 ± 10.91	P < 0.0001
Serum Creatinine (mg/dl)	1.34 ± 0.27	0.75 ± 0.12	P < 0.0001
FT3(pmol/L)	1.35 ± 1.09	4.06 ± 0.86	P < 0.0001
FT4(ng/ml)	0.49 ± 0.23	1.09 ± 0.38	P < 0.0001
TSH(µIU/ml)	25.05 ± 8.96	3.96 ± 1.22	P < 0.0001

Graph 1: Comparison between levels of serum Homocysteine, total Cholesterol, Serum Creatinine, Free T3, Free T4 and thyroid stimulating hormone in overt hypothyroidism case and control group



The Table and Graph showed the increased Homocysteine (26.62 ± 6.14) in hypothyroidism patient if compared with the control group (10.30 ± 3.84). The level of total cholesterol was significantly higher (211.71 ± 25.28) in the hypothyroidism patient when compare with the control group (103.87 ± 10.91) who had reduced Cholesterol level. Our study showed the increased Serum Creatinine (1.34 ± 0.27) in hypothyroidism patient as compared to the control group (0.75 ± 0.12).The level of FT3was significantly reduced (1.35 ± 1.09) in the hypothyroidism patient when compare with the control group (4.06 ± 0.86) who had reduced FT3 level. FT4 in control group were higher (1.09 ± 0.38) as compare to overt hypothyroidism patient (0.49±0.23), which was statistically highly significant. The level of TSH was significantly higher (25.05±.96) in the hypothyroidism patient when compare with the control group (3.96±1.22) who had reduced TSH level.

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DISCUSSION

Raised plasma total homocysteine was found to be closely correlated with hypothyroidism in this study. As shown in Table 1, serum tHcy levels in hypothyroidism patients were significantly higher than in the control group (p 0.0001). This inference is backed by a number of previous studies **(Saleh A. Bamashmoos et al. 2013; Gunduz et al. 2012,Diekman et al., 2001; Lien et al., 2000)**. [25-28]

Thyroid hormones have a direct effect on tHcy metabolism in the liver and clearance in the kidney, so elevated tHcy levels may be the result of one of two mechanisms: increased tHcy formation or decreased renal tHcy clearance. **(Saleh A. Bamashmoos et al. 2013; Orzechowska et al., 2005).**[25, 29]

However, in line with previous study, we discovered that serum creatinine was significantly higher in hypothyroid patients than in the control group. Hypothyroidism has been related to a rise in serum creatinine levels, which can be lowered with thyroid hormone replacement **(Diekman et al., 2001)**. (27) The mild increase in creatinine may be explained by thyroid hormones' direct effect on renal function, tHcy metabolism, and kidney clearance. (.**(Hollander et al., 2005; Nakahama et al., 2001).**[28,29]Low renal tHcy is caused by impaired renal tHcy metabolism, which results in a lower glomerular filtration rate (GFR) and higher serum creatinine. **(Hollander et al., 2005; Nakahama et al., 2001).**[30,31]

In our research, patients with hypothyroidism had significantly higher serum mean total cholesterol levels than the control group. These findings were in line with expectations **(Gunduz et al., 2012; Yazbeck et al., 2001; Lien et al., 2000)**. [26,9,28] Elevated serum cholesterol could be due to the effects of thyroid hormones on cholesterol metabolism or disposition **(Ness and Lopez, 1995)**,[32]which could intensify the connection between hypothyroidism and hypercholesterolemia, or it could be due to the effects of Hcy on cholesterol production and secretion, because Hcy stimulates cholesterol production and secretion in hepatic cells **(Karmin et al., 1998)**.[33]Since hypercholesterolemia may lead to increased cardiovascular morbidity, it cannot fully explain accelerated atherosclerosis, increased serum tHcy, and cholesterol levels in hypothyroid patients, all of which contribute to an increased cardiovascular risk. Studies on assessments of homocysteine were reported by Sinha et. al. [34] and Memon et. al. [35]. Studies related to creatinine assessment were reviewed [36-38]. Taksande reported about sensory nerve conduction study in patient of thyroid dysfunction in Central India[39]. Wagh et. al. reflected on relationship between hypothyroidism and body mass index in women[40]. Jose et. al. studied profile of thyroid dysfunctions among the female population in a rural community[41]. Studies by Dakhode et. al [42] and Regmi et. al. [43] reflected on similar problems in different groups.

CONCLUSION

In conclusion, our results of elevated serum tHcy, T. cholesterol, and creatinine in overt hypothyroidism were confirmed by our studies. Higher tHcy levels can increase the risk of cardiovascular disease. Along with hypercholesterolemia, hyperhomocysteinemia can explain these patients' accelerated atherosclerosis. Thyroid hormones may have a direct effect on renal function, tHcy metabolism, and kidney clearance, which could explain the elevated serum creatinine. Estimation of tHcy, total cholesterol, and creatinine in hypothyroid patients may play a significant role as a possible risk factor for accelerated atherosclerosis and cardiovascular disease, according to our findings.

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