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ORIGINAL RESEARCH

To Study Serum HDL Level in Subclinical Hypothyroidism and Its Association with TSH: A Case Control Study

[1]Nehal Patel,[2]Nitish Thakur, [3]Sahil Chhabra, [4]Sevy Puri,[5]Luqman Hafeez, [6]Kiran Kumar Singal

[1,3,4,5]Junior Resident, [2]Assistant Professor, [6]Professor, Department of Medicine, Maharishi Markandeshwar Medical College and Hospital,Kumarhatti, Solan, Himachal Pradesh, India

Correspondence:
Nehal Patel
Junior Resident, Department of Medicine, Maharishi Markandeshwar Medical College and Hospital,Kumarhatti, Solan, Himachal Pradesh, India
Email:docnehal2510@gmail.com

ABSTRACT

Objectives:1)To study level of serum highdensity lipoprotein (HDL) level in subclinical hypothyroidism andeuthyroid patients 2) To study association between serum HDL and serum TSH in subclinical hypothyroidism.

Materials and Methods:The study was hospital based observational study which included15 patients of subclinical hypothyroidism and 15 patient's euthyroid after diagnosis based on theirserum thyroid stimulating hormone (TSH), freeT3 and freeT4 level done during their regular visit to outpatient medicine department.B**loodsample was collected of all the participants after an overnight (12hours) fasting and serum high density lipoprotein levels was estimated. Statisticalanalysis was done on collected data.**

Results: Participants with euthyroidism and subclinical hypothyroidism showed no significant difference in serum high density lipoprotein levels and a negative correlation was found between serum TSH and serum HDL level in subclinical hypothyroidism group.

Conclusions:Thyroid hormones have various effects on lipid metabolism.The effects of subclinical hypothyroidism on serum HDL level were not statistically significantand a negative correlation between serum TSH and serum HDL which was suggestive of linear decrease in serum HDL with increase in serum TSH levels.

Keywords: Serum TSH, Free T3, Free T4, Serum HDL, Subclinical Hypothyroidism.

INTRODUCTION

Among endocrine disorder thyroid disorder prevalence has increased in recent years, specifically hypothyroidism and hyperthyroidism, detected either clinically or subclinically. Thyroid hormone is linked to multiple metabolic disorders due to the impact of thyroid hormones on protein, carbohydrate, and lipid metabolism which regulates basal energy expenditure and may directly or indirectly result in changes in other regulating hormones like insulin or catecholamines.[1] Thyroid dysfunction is defined as a change in serum TSH levels in the presence of abnormal or normal thyroid hormones. Subclinical hypothyroidism is defined as normal levels of circulating T3 and T4 with increase in serum TSH.[1] Dyslipidemia in patients with thyroid disorder is a common metabolic abnormality, whether the disease is overt or subclinical form the effect of thyroidhormones affect in all aspects of lipid metabolism leading to various qualitative and/or qualitative changes of cholesterol, phospholipids, triglycerides and other lipoproteins.[2]Lipid metabolismincluding synthesis,

mobilization, and degradation all aspects is influenced by thyroid hormone. Dyslipidemia consisting of high levels of total cholesterol and LDL cholesterol is a common finding in clinicalhypothyroidism patients.[2,3]Thyroid hormones affect hepatic lipase activity and cholesteryl ester transfer protein, which are decreased in hypothyroidism and increased in hyperthyroidism, with consequent changes not only in total high-density lipoprotein (HDL) but also in HDL subfraction levels.[4] By binding to the thyroid hormone receptor, thyroid hormone through a competitive action inhibit the liver X-receptor-mediated ATP-binding cassette transporter A1 gene expression, and result in decrease level of HDL in hyperthyroidism patients and increase level of HDL in hypothyroidism patients.[5,6]In many studies it is established thatsubclinical hypothyroidism is a risk factor for hypercoagulable state, insulin resistance, low grade inflammation and altered lipid metabolism.[7]In hypothyroidism, decrease in thyroid hormone level results in decrease of bile acid flow which further increases intrahepatic cholesterol despite the decrease hepatic uptake of cholesterol from circulation.[8]In parallel decrease hepatic uptake of LDL by LDL receptor and lowering of cholesterol excretion. The result appears to be decrease in cholesterol catabolism and excretion which lead to secondary dyslipidemia in hypothyroidism patients.[9]It is difficult to differentiate whether patient is having mild thyroid failure or transient thyroid gland function disturbances. In autoimmune thyroiditis and subacute thyroiditis transient hypothyroid stateis followed by euthyroid state in these patients evidence has shown on long term follow up development of permanent hypothyroidism. Persistent subclinical hypothyroidism diagnosis can be verified after 6-12 months on reevaluating TSH concentration.[10]

MATERIALS AND METHODS

The present study was a single centre, prospective, observational, hospital-based study which was conducted on patients including 15 patients of euthyroidism and 15 patients of subclinical hypothyroidism from outpatients of medicine department at MMMC&H Kumarhatti, Solan. Patients aged 18 to 65 years, without known thyroid dysfunction, not on any treatment altering thyroid level were included in the study during their routine clinical visit after diagnosis by measuring free T3, free T4 and TSH level with the help of the Siemens ADVIA Centaur XP immunoassay system, using the Chemiluminescence immunoassay (CLIA) method.

FreeT3 (0.92-11.25 pg/ml)

Free T4 (0.89-1.76 ng/dl) and

TSH level(0.4-4.2μIU/ml) (Reference ranges taken from institutional reference range)

Euthyroid if thyroid hormone levels fall within reference range and Subclinical hypothyroidism will be considered if TSH >4.2 μIU/ml and free T3 and free T4 within reference range.

In all 30 patients early morning fasting (12 hours) blood samples was collected and was analyzed for serum HDL level by standard enzymatic methods.

INCLUSION CRITERIA

Patients aged 18-65 years

Not a known case of thyroid dysfunction or not on any treatment altering thyroid level

EXCLUSION CRITERIA

Patients on antithyroid drugs or radioiodine treatment.

Patient with a known history of dyslipidemia on medication.

Patients with a H/O jejunoileal bypass, biliopancreatic diversion, extensive small bowel resection, total parenteral nutrition

Patient on weight loss therapy or steatogenic drugs

Known HIV- positive case

STATISTICAL ANALYSIS

The data was analysed using Microsoft Excel and SPSS and pvalue was calculated and Pearson's correlation was calculated.

Table 1: Base line characteristic and biochemical parameters of study groups

Parameters	Euthyroid(n=15) Mean±SD	Subclinical Hypothyroidism (n=15) Mean±SD
Age(years)	49±10.7	44±11.4
Gender	Male-4	Male-3
	Female-11	Female-12
BMI(kg/m^2)	20.13±3.8	28.12±4.26
Free T3(pg/ml)	2.09±1.1	2.72±2
Free T4(ng/dl)	1.6±1.1	1.67±1.6
S. TSH(µIU/ml)	2.43±1.3	7.9±2.8
S. HDL(mg/dl)	38.8±4.8	37.8±4.8

Table 2: Comparison of serum HDL and serum TSH level in euthyroid and subclinical hypothyroid patients

	Euthyroid	Subclinical hypothyroidism	P-value
S. HDL (Mean ± SD)	38.8±4.8	37.8±4.8	0.25
S.TSH (Mean ± SD)	2.43±1.3	7.9±2.8	0.0001

P value <0.05 is significant

Table 3: Correlation of serum HDL and serum TSH in subclinical hypothyroidism patients

No. of patients	Serum HDL	Serum TSH	r value	Correlation
15	37.8±4.8	7.9±2.8	-0.211	Negative

RESULTS

In our study mean age of patients in euthyroid group was 49±10.7years and in subclinical hypothyroidism group was 44±11.4 years.A female has higher prevalence of thyroid dysfunction in subclinical hypothyroidism group 12 female patients and 3 male patients.Mean BMI in euthyroid group was 20.13±3.8kg/m^2 and in subclinical hypothyroidism was 28.12±4.26 kg/m^2.In present study free T3 level in euthyroid patients was 2.09±1.1pg/ml and in subclinical hypothyroidism group was 2.72±2pg/ml. Mean free T4 level in euthyroid patients was 1.6±1.1ng/dl and in subclinical hypothyroidism patients was 1.67±1.6ng/dl.

Serum TSH level in euthyroid patients was 2.43±1.32µIU/ml and in subclinical hypothyroidism patients was 7.9±2.82 µIU/ml. In our study mean serum HDL in euthyroid group was 38.8±4.8mg/dl and in subclinical hypothyroidism was 37.8±4.8 mg/dl (P value is 0.25) i.e. not statistically significant.The spearman's correlation coefficient was used for relationship between serum TSH and serum HDL level in subclinical hypothyroidism group. Serum TSH levels were negatively correlated with HDL(r=-0.211) in subclinical hypothyroidism which was suggestive that there was linear increase in TSH level with decrease in HDL level .

DISCUSSION

The current study was undertaken at MMU, Solan in which serum HDL level was done in 15 euthyroid patients and 15 subclinical hypothyroid patients on routine clinical visit to outpatient department of medicine. The mean serum HDL cholesterol was not significantly decreased in subclinical hypothyroidism compared to the euthyroidism(*P*=0.25). The mean serum HDL level was38.8±4.8mg/dl in euthyroid group and in subclinical hypothyroidism was 37.8±4.8mg/dl. Althaus BU et al. in his study found that evaluate the lipid profiles in patients with subclinical (n = 52) and overt hypothyroidism (n = 18) in comparison to normal controls (28 and 18, respectively). In subclinical hypothyroidism there was decrease in HDL and increased LDL concentration. Total cholesterol and triglyceride concentrations were unaltered.[11]Huesten WJ et al. in the study found that participants fulfilling criteria meeting for subclinical hypothyroidism had increasedmean cholesterol levels (226 vs 217 mg/dL,P = .003) and increased cholesterol levels (74.2% vs 63.9%, P = 0.02) than the euthyroid group, but there were no significant differences in high-density lipoprotein (HDL) levels or low-density lipoprotein (LDL) . When adjusted for confounding variables and the useof lipid-lowering drugs, however, subclinical hypothyroidism was not related toelevations in cholesterol levels, LDL levels,or triglyceride levels or to a low HDLlevel.[12] Rastgooye Haghi A et al. in his study which included 53 patients with subclinical hypothyroidism and 53 euthyroid cases found that Participants with subclinical hypothyroidism had significantly higher LDL and lower HDLlevels than the control group regardless of age group and gender (P-value <0.001),but there was no difference in triglycerides and total cholesterol levels (P-value <0.05). Theprevalence of dyslipidemia and subclinical hypothyroidism was only significant in females.[13] In our study also similar results was found there was higher prevalence of subclinical hypothyroidism in females. Kosuke Inoue et al. in his studyfound association between higher TSH levels and increased risk ofall-cause mortality. Cardiovasculardisease mediated 14.3% and 5.9% of the association of subclinicalhypothyroidism and high-normal TSHconcentrations with all-cause mortality,respectively in which median duration of follow-up for mortality ascertainment was 7.3 (interquartile range, 5.4–8.3) years, during which 435 deaths from all causes were identified.[14]In our study when correlation coefficient was calculated between serum HDL and serum TSH the linear correlation was -0.21 which showed that with increase in serum TSH level there was linear decrease in serum HDL.Bjorn O A Svold et al. found that within the reference range of TSH, there was a linear and significant increase in total serum cholesterol, LDL cholesterol, non-HDL cholesterol and triglycerides, and a linear decrease in HDL cholesterol with increasing TSH.[15]

CONCLUSION

Thyroid hormones have various effects on lipid metabolism. The effects of subclinical hypothyroidism on serum HDL level were not statistically significant and a negative correlation between serum TSH and serum HDL was found.

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