



Research Article

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Study of serum apolipoprotein A1 and HDL cholesterol in subclinical hypothyroidism

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ABSTRACT

Subclinical hypothyroidism is one of the most common endocrine disorders in India. As thyroid hormones have effect on lipid metabolism, subclinical hypothyroidism may lead to significant dyslipidemia. Dyslipidemia is a major risk factor for atherosclerosis and ischemic heart disease. This study was done to see the levels of serum Apolipoprotein A1 (Apo A1) and HDL cholesterol levels among subclinical hypothyroid patients and healthy euthyroid controls. Study involved 35 subclinical hypothyroid cases and 35 age & sex matched healthy euthyroid controls. Serum Apo A1 and HDL cholesterol levels were measured by commercially available kits. Statistical analysis was done with Students't- test and Pearson correlation using SPSS 17.0. Serum Apo A1 and HDL cholesterol were significantly low in subclinical hypothyroid cases compared with controls ($p < 0.001$). Serum Apo A1 and HDL cholesterol were significantly negatively correlated with serum TSH levels ($p < 0.05$). This study suggests that, serum Apo A1 and HDL cholesterol levels are significantly reduced in subclinical hypothyroidism patients. As these dyslipidemic changes are strongly associated with occurrence of ischemic and metabolic diseases, it is beneficial to timely detect and control dyslipidemia in such patients.

Key words: Apolipoprotein A1, dyslipidemia, high density lipoprotein cholesterol, subclinical hypothyroidism.

INTRODUCTION

Thyroid disorders are one of the most common endocrine disorders in India. The total burden of thyroid disorders in India is 42 million. This includes subclinical & overt cases of hypo & hyperthyroidism [1]. Prevalence of thyroid diseases in female is more than in male. Subclinical disease is more prevalent than overt disease [2].

Clinical features of subclinical hypothyroidism are vague and nonspecific. Some people have no symptoms while some people may present with easy fatigue, sluggishness, weight gain, constipation etc. Therefore presence of disease might go unnoticed in large number of people. Diagnosis is mainly based on increased level of serum TSH (Thyroid stimulating hormone) with normal levels of serum T3 & T4 [3].

Thyroid hormones have significant effects on regulation of lipid synthesis, absorption and metabolism. The composition and the transport of lipoproteins are disturbed significantly in thyroid diseases [4,5]. Dyslipidemia caused due to subclinical hypothyroidism has been claimed to be a risk factor for atherosclerosis and coronary artery diseases [6]. Subclinical hypothyroidism could impair vascular function by inducing an increase in systemic

vascular resistance, arterial stiffness and altering endothelial function, thereby potentially increasing the risk of atherosclerosis and coronary artery disease [7].

HDL (High Density Lipoprotein) cholesterol is one of the major anti atherogenic factor. HDL is synthesized from liver and small intestine containing Apo-A1 (Apolipoprotein A1) as major apolipoprotein. Apo-A1 is an activator of LCAT (Lecithin cholesterol acyl transferase). Cholesterol from peripheral tissues is converted to cholesterol ester by LCAT and taken inside HDL particle which is later taken up by liver for disposal. Decreased HDL cholesterol is associated with increased deposition of cholesterol in peripheral tissues and increased incidence of atherosclerosis and ischemic heart disease [8].

This study was undertaken to study and compare changes in serum Apo-A1 level & HDL cholesterol level in subclinical hypothyroidism cases and healthy euthyroid controls

EXPERIMENTAL SECTION

A case control study was carried out taking 35 subclinical hypothyroidism patients as cases and 35 healthy euthyroid age and sex matched controls. Study subjects were selected from Bapuji Hospital and Chigateri Hospital, Davangere (both these hospitals are attached to teaching institute, J.J.M. Medical College, Davangere). Informed consent was taken from each participant and this study was approved by the institutional ethical committee of J.J.M. Medical College, Davangere to use human subjects in the research study. A proforma was used to note demographic details of study subjects.

A) Selection of study subjects

35 newly diagnosed patients of subclinical hypothyroidism in the age group of 18–70 years were taken as cases. Patients attending outpatient department of medicine were screened for subclinical hypothyroidism and thyroid profile was done from suspected cases. Based on the result, patients with elevated serum TSH levels ($> 5.45 \mu\text{IU/ml}$) with normal serum T_3 (0.5 – 2.0 ng/ml) and normal serum T_4 (4.4-10.8 $\mu\text{g/dl}$ in males; 4.8-11.6 $\mu\text{g/dl}$ in females) levels were diagnosed as subclinical hypothyroidism [2]. Later in these patients, Apo A-1 and HDL levels were estimated. Patients with overt hypothyroidism, those who were on treatment with thyroxine, hypolipidemic drugs, antihypertensives, steroids, patients suffering from renal, liver, cardiovascular disease and diabetes mellitus excluded from the study

Controls: 35 age and sex matched healthy euthyroid subjects.

B) Collection and preparation of blood samples: Under all aseptic precautions, about 3 ml of venous blood was drawn in a sterile bulb from selected subjects after a period of overnight fasting of 12 hours. Serum was separated by centrifugation and was used for analysis. Serum was stored at -20°C until assayed.

C) Analysis of serum samples:

Concentration of serum ApoA-1 was analyzed by immunoturbidimetry method [9] and HDL cholesterol was analyzed by phosphotungstic acid & enzymatic cholesterol oxidase- phenyl aminoantipyrine (CHOD-PAP) method [10]. The analytical kits were procured from Erba Diagnostics Mannheim GmbH and analysis was done in semi-autoanalyzer (CHEM-5 Plus V₂, Erba Mannheim).

Statistical analysis:

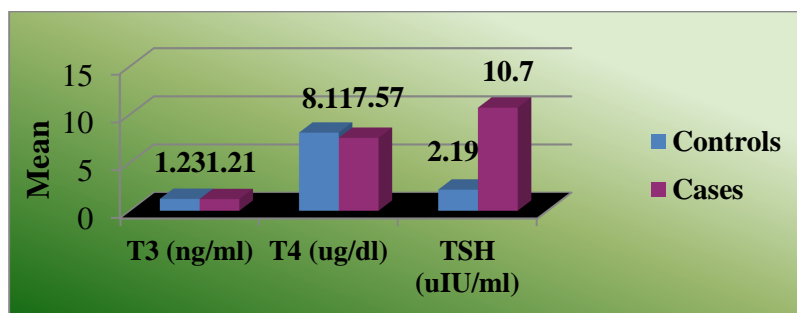
Descriptive data are presented as mean \pm SD and range values. To evaluate statistical difference, Students unpaired 't' test was used. Pearson's correlation coefficient was used to assess the relationship between the parameters. The statistical software SPSS 17.0 was used for analysis of the data. For all the tests, the probability value (p-value) of less than 0.05 was considered statistically significant.

RESULTS AND DISCUSSION

Graph 1 shows that the mean levels of serum TSH were higher in subclinical hypothyroidism cases than controls and this difference is statistically highly significant (p value < 0.001). Table 1 shows that subclinical hypothyroidism is more prevalent in female compared with male. As shown in table 2, there was no significant difference in age between cases and controls. Serum TSH levels were significantly higher in cases & serum HDL cholesterol and Apo AI were significantly lower in cases compared with controls (p < 0.001). As shown in graph 2 & 3, serum HDL & Apo AI are negatively correlated with serum TSH levels (p < 0.05).

Table 1: Gender distribution in study groups

Groups	Female	Male	Total
Cases	26 (74%)	9 (26%)	35
Controls	25 (71%)	10 (29%)	35

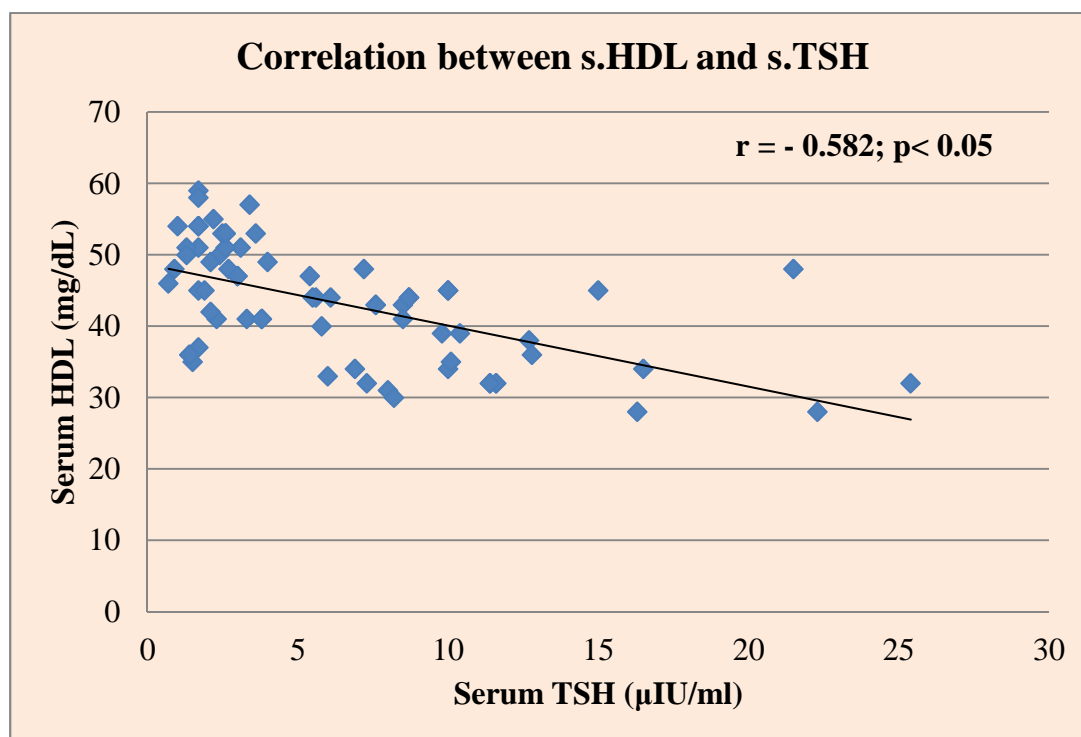


Graph 1: Comparison of serum T₃, T₄ and TSH levels among study subjects

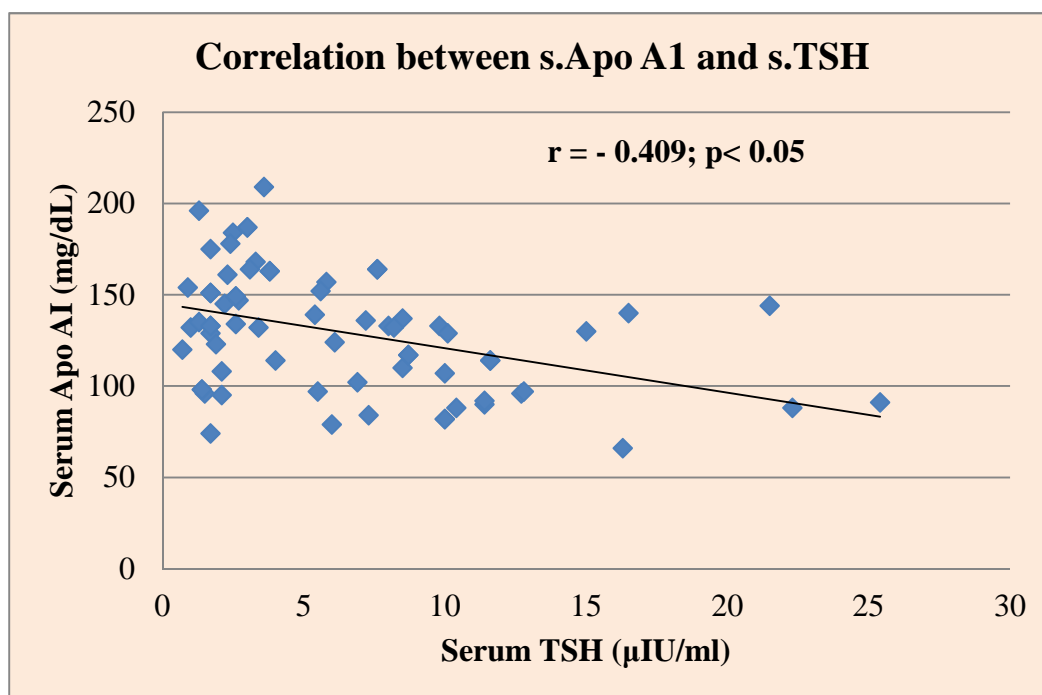
Table 2: Comparison of different parameters between cases and controls

Groups		Age (Years)	TSH (μIU/ml)	HDL cholesterol (mg/dl)	Apo A-I (mg/dl)
Cases	Mean ± SD	37.31 ± 11.01	10.70 ± 4.85	38.25 ± 6.20	115.05 ± 26.37
Controls	Mean ± SD	37.02 ± 13.63	2.19 ± 0.88	48.02 ± 6.50	143.85 ± 31.89
Cases Vs Controls	p value*	0.923	< 0.001	< 0.001	< 0.001

*Unpaired students t test, $p < 0.001$ highly significant, $p > 0.05$ non significant.



Graph 2: Pearson’s correlation between serum HDL cholesterol and serum TSH among study subjects



Graph 3: Pearson's correlation between s. Apo A1 and s. TSH among study subjects

This study shows comparison of serum Apo A1 & HDL levels among subclinical hypothyroid cases and healthy euthyroid controls. As per observation in our study, subclinical hypothyroidism was more prevalent among females than males. This finding is in accordance with studies done by Elizabeth Haket al [11] and Abraham R et al [12]. Age and gender are major factors affecting lipid profile. Advancing age has more probability of having dyslipidemic changes in their lipid profile. Male and female tend to have different lipid profile [13]. Therefore age and sex matched study groups were selected to remove the effect of these confounding factors.

In our study, serum TSH levels were significantly elevated in subclinical hypothyroid cases compared with euthyroid controls. Elevation in TSH can be the earliest sign of impending thyroid gland failure. Initially thyroid hormone levels are maintained by increasing production of TSH but later on as subclinical disease progresses to overt disease, TSH elevation becomes no longer effective to maintain thyroid gland output and features of hypothyroidism become clinically visible [14,15].

Thyroid hormones have great impact on lipoprotein metabolism. Thyroid dysfunction can alter patient's lipid profile significantly [16]. In our study, we found significantly decreased serum HDL cholesterol and Apo A1 levels in subclinical hypothyroid cases compared with euthyroid controls. These findings are in accordance with studies done by many researchers [17-19].

Apo A-I is the major protein in HDL cholesterol. It plays an important role in protection against atherosclerosis by providing a shuttle mechanism that transports cholesterol from extrahepatic tissues to the liver for processing to bile acids [20]. Thyroid hormones increases the expression and concentrations of apo A-I protein. Levels of apo A-I are strongly correlated with those of HDL cholesterol. Thus, thyroid hormones may promote the synthesis of HDL cholesterol and thereby increase the initial step of reverse cholesterol transport [21]. Decreased thyroid hormones are associated with decreased lipoprotein lipase activity leading to increased serum triglycerides levels [4, 16]. Elevated serum triglycerides are associated with increased catabolism of HDL particles [22, 23]. All these factors combine together and lead to decreased level of HDL and Apo A1 in subclinical hypothyroid patients.

In our study, we found that serum HDL cholesterol and Apo A1 level is negatively correlated with serum TSH. As disease severity increases, serum TSH increases and correspondingly HDL cholesterol and Apo A1 reduces. Thus, more severe disease is associated with lower HDL level and more significant dyslipidemia.

Decreased level of serum HDL cholesterol is strongly associated with increased prevalence of atherosclerosis, ischemic heart diseases, cerebro-vascular disease etc. Dyslipidemia is also a strong risk factor for metabolic diseases such as metabolic syndrome & diabetes mellitus [24]. Several studies have proved timely intervention with L-

thyroxine (L-T₄) therapy can reduce and reverse the metabolic changes in subclinical hypothyroidism patients. Regular L-T₄ therapy can bring back the dyslipidemic changes to normal in such patients [17, 25].

Thus, it is advisable to rule out dyslipidemia in subclinical hypothyroid patients. As timely diagnosis and intervention with L-T₄ can postpone or reverse metabolic changes in such patients and can reduce the risk of metabolic and ischemic diseases.

CONCLUSION

This study suggests that, serum HDL cholesterol and Apo A1 levels are significantly reduced in subclinical hypothyroidism patients. Such dyslipidemic changes are strongly associated with occurrence of ischemic and metabolic diseases. Early diagnosis and treatment may reduce the dyslipidemia and associated risk of diseases.

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