**ORIGINAL ARTICLE**

# High Density Lipoprotein Status in Hyperthyroid, Hypothyroid and Euthyroid Conditions in Pakistani Population

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## ABSTRACT

**Aim:**To determine the serum HDL cholesterol status in different states of thyroid gland activity, before and after the treatment of thyroid dysfunction.
**Study Design:**Analytical cross sectional study.
**Place and Duration of study:**The present study was conducted at the Institute of Molecular Biology and Biotechnology, University of Lahore, Defence Road Campus Lahore. The experimentation was also undertaken at the Institute of Nuclear Medicine and Oncology (INMOL) Lahore.
**Methods:** Serum thyroid hormones were assayed by the Radioimmunoassay at the Institute of Nuclear Medicine and Oncology Lahore (INMOL). Serum HDL-C was measured by direct homogenous assay.
**Results:** In patients with subclinical hypothyroidism, serum HDL-C was slightly increased than controls ($P > 0.05$). In hypothyroid state, the condition resulted due to medication of hyperthyroidism, level of HDL-C decreased ($P > 0.05$). Thyroxine treatment decreased the HDL-C in hypothyroid subject in comparison to the diseased state ($P > 0.05$). Hyperthyroidism was associated with slight decrease in the concentration of HDL-C than the controls ($P > 0.05$).
**Conclusion:** Hypothyroidism and hyperthyroidism have opposite effects on serum HDL-C.Hyperthyroidism resulted in a decreased HDL –C while hypothyroidism resulted in increased HDL-C. After the treatment of hypothyroidism and hyperthyroidism HDL-C decreased in both the conditions.
**Keywords:** Radio immune assay. Thyroiditis.High density lipoprotein.Hyperthyroidism,

## INTRODUCTION

Thyroid hormone plays an important role in hepatic lipid homeostasis[1]. Thyroid hormones are involved in regulation of lipid and lipoprotein metabolism. Therefore, thyroid dysfunction is reported to induce significant changes in lipid and lipoprotein metabolism. It is however apprehended that lipid disorders in thyroid dysfunctions exhibit great individual variability and the pattern of changes in lipid fractions in thyroid disorder remain controversial[2]. Hypothyroidism and hyperthyroidism have contrasting effects on plasma lipids and apo-lipoproteins[3]. The changes in HDL-C and LDL-C correlate with changes in FT4 after the transition of hyperthyroid and hypothyroid state to euthyroidism[4]. The plasma concentrations of total cholesterol, HDL-C, total/HDL-C ratio, phospholipids, apo A-I, and apo B were decreased in hyperthyroidism whereas triglyceride (TG) and apo E concentrations did not change significantlyduring therapy[3,4].

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Overt and sub clinical hypothyroidism had an adverse effect on the serum lipid profile that may predispose the development of atherosclerotic disease[6]. In hypothyroidism, total and HDL cholesterol, total/HDL cholesterol ratio, apo AI and apo E was elevated[3]. Sub clinical hypothyroidism had higher total cholesterol and LDL-C levels compared with euthyroid controls. No significant changes in serum TGs and HDL-C levels were observed except a decreasing trend in HDL-C and an increasing trend in TGs[7].

Thyroid hormones can affect several proteins related with HDL-C metabolism such as hepatic lipase (HL), lecithine cholesterol acetyl transferase (LCAT), cholesterol ester transfer protein (CETP) and possibly scavenger receptor BI (SR-BI)[8]. The present research was done to determine the status of HDL-C in different thyroid disease states in Pakistani population.

## MATERIALS AND METHODS

The present study was conducted at the Institute of Molecular Biology and Biotechnology, University of Lahore, Defence Road Campus Lahore. The experimentation was also undertaken at the Institute of Nuclear Medicine and Oncology (INMOL) Lahore. Authorization for blood sampling was obtained from

patients by University Ethical Committee of Institute of Molecular Biology and Biochemistry (IMBB) and the Code of Ethics of the World Medical Association were followed. One hundred and twenty individuals (20 control and 100 with thyroid problem) were included in the study. Twenty patients were taken in each of the treatment group.

Medical history of all patients was taken prior to blood collection. Blood samples were left for 2 hours at room temperature to separate the serum from blood cells. Blood samples were centrifuged at 50,000 rpm for 5 minutes to obtain clear serum. Samples were kept in the freezer maintained at -20$^{o}$C till analysed.

Patients who participated in this study were divided into five groups randomly as: Controls (age, 35.5±3.90); Hyperthyroid therapy group (age, 36.25±4.97); Euthyroid after hyperthyroid medication (age, 39±6.2); Hypothyroid group (age, 47.6±4.7); Euthyroid after hypothyroid treatment (age, 38.6±4.1); Transition of hyperthyroid to hypothyroid state (age, 37.8±3.9). 50-150 µg/day of thyroxine given to the hypothyroid patients. 8-15 mCi of radioactive iodine was injected to the hypothyroid patients. Hyperthyroid patients were treated with neomeracazole (carbimazole) in 50-150 mg/TDS.

Statistical analysis was done with SPSS ver16.0. Parametric values were given as the mean±SE. Thyroid function test values and serum HDL-C values of patients and control group were compared by one-way ANOVA.

## RESULTS

Table 1 show subclinical hypothyroid subjects displayed non significantly high levels of HDL-C when compared to the controls (P>0.05). Level of T4 and T3 were almost similar controls (P>0.05). TSH concentration of hypothyroid subjects was significantly higher (8.659±0.91218) than the control TSH (2.2816±0.37639; P<0.05). Treatment of hypothyroidism slightly decreased the serum HDL-C hypothyroid state (45.5286±2.36892 and 53.6243±1.45886; P<0.05). The transient hypothyroid patients who had hypothyroid after hyperthyroid treatment, also showed the low levels of HDL-C when compared hypothyroid subjects (45.2406±1.73676 and 53.6243±1.45886; P<0.05) and non significant lower values than the control and euthyroid state. Treatment of hypothyroidism did not alter the T4 and T3 concentration (P>0.05) when compared to the control and hypothyroid subjects. Transient hypothyroid showed the values (P>0.05) not significantly different from other groups. Treatment of hypothyroidism significantly reduced the TSH concentration than the hypothyroid state (2.0729±0.50935 and 8.6593±0.91218: P<0.05).In transient hypothyroid group TSH level was high than control (9.91983±1.68371 and 2.2810±0.37639; P<0.05) and euthyroid (9.91983±1.68371 and 2.0729±0.50935; P<0.05) and non-significant difference were found from hypothyroid subjects.

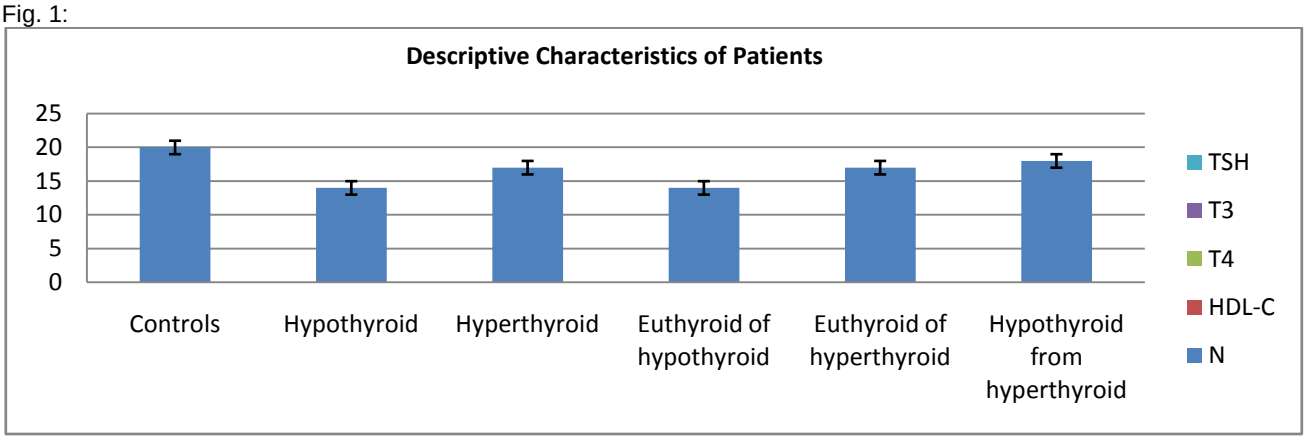
HDL-C of hyperthyroid was lower than the controls (P>0.05). T4 (37.5941±1.80666 and 16.7800±0.84640; P<0.05) and T3 (16.9400 ± 1.65545 and 3.5540±0.37390; P<0.05) concentration in hyperthyroid group was significantly higher than the controls.TSH value inhyperthyroid group decreased than the controls (P>0.05). Treatment of hyperthyroidism non-significantly decreased the HDL-C as compared to the hyperthyroid state (P>0.05). In transient hypothyroid group, HDL-C level was lower as compared to the control (P>0.05) and hypothyroid subjects (45.2406±1.73676 and 51.7400±2.01595; P>0.05). T4 (15.6353±0.54428 and 37.5941±1.80666; P<0.05) and T3 (4.2300±0.19154 and 16.9400±1.65545; P<0.05) significantly decreased after the treatment. T4 and T3 were decreased than controls and hyperthyroid group (P>0.05) in transient hypothyroid subjects. Hyperthyroid treatment slightly increased the TSH level. In transient hypothyroid patients significantly high level of TSH than the control group was recorded (9.91983±1.68371 and 2.2810±0.37639;P<0.05).

Table 1: Descriptive characteristics of patients

| | n | HDL-C | T4 | T3 | TSH |
|---|---|---|---|---|---|
| Controls | 20 | 51.7400 ± 2.01595 | 16.7800 ± 0.84640 | 3.5550 ± 0.37390 | 2.2810 ± 0.37639 |
| Hypothyroid | 14 | 53.6243 ± 1.45886 | 15.0571 ± 0.46406 | 3.4050 ± 0.31030 | 8.6593 ± 0.91218 |
| Hyperthyroid | 17 | 49.4700 ± 3.09306 | 37.5941 ± 1.80666 | 16.9400 ± 1.65545 | 0.259 ± 0.00228 |
| Euthyroid of hypothyroid | 14 | 45.5286 ± 2.36892 | 17.1193 ± 0.68836 | 3.6743 ± 0.12350 | 2.0729 ± 0.50935 |
| Euthyroid of hyperthyroid | 17 | 37.8371 ± 2.46871 | 15.6353 ± 0.54428 | 4.2300 ± 0.19154 | 1.0506 ± 0.22142 |
| Hypothyroid from hyperthyroid | 18 | 45.2406 ± 1.73676 | 9.9594 ± 1.04593 | 3.4667 ± 0.38652 | 9.1983 ± 1.68371 |

[1]University of Lahore, Lahore, Pakistan

Fig. 1:




## DISCUSSION

This study provided an opportunity to observe the association of thyroid dysfunction and its effects on serum HDL-C.Thyroid dysfunction has a marked effect on the distribution of HDL particles. In subclinical hypothyroidism (SCH) metabolism of triglyceride-rich lipoproteins was normal while abnormalities were found in HDL metabolism that were reversed by LT4 treatment[9]. It has been reported by different researchers that HDL-C metabolism is altered in thyroid disorders. Alteration in HDL-C and other lipoproteins in different thyroid disorders are still controversial. Effect of thyroid hormone on HDL-C was facilitated mainly because of its influence on hepatic lipase activity[10]. Recent work indicates the effect of thyroid dysfunction on concentration of serum HDL-C. Our data cleared the increased levels of serum HDL-C in subclinical hypothyroid patients when compared to the controls. Heimberget al[11]and Brien et al[3]also reported the high levels of HDL-C in hypothyroid subjects. In subclinical hypothyroid, HDL-C was decreased when compared to control[12]. HDL-C in subclinical hypothyroidism did not differ significantly as compared to euthyroid[13]. Thyroid hormone affects the expression of the HDL binding site in liver cells which may be the reason of decreased HDL clearance in the hypothyroid[14].

The results of the present study predicted the decreased concentration of HDL-C in hyperthyroidism compared to control. Our results are in accordance with different previous work. HDL-C was decreased in hyperthyroid state when compared to control[15,3]. Conversely Ariehet al[16]stated that HDL-C was unchanged as compared with controls in hyperthyroidism. Hepatic lipase (HL) and lipoprotein lipase (LPL) are both essential determinants of plasma HDL concentrations. It was suggested that an increased hepatic lipase (HL) activity may contribute to the lower HDL levels in hyperthyroid patients[17].

The influence of thyroxine treatment on HDL-C might reflect changes in HDL composition due to the multiple effects of thyroid hormones on lipid metabolism[18]. In our research decreased HDL-C concentration was recorded when compared to the hypothyroid and controls. Our findings are in confirmation to the previous studies of Friis and Pedersen[19]. Similar findings were reported by Brien et al[3] that HDL-C decreased with treatment of hypothyroidism. The change in HDL-C correlated with the increase in hepatic lipase activity[10,18].

Treatment of hyperthyroidism, in our study revealed moderately decreased concentration of serum HDL-C compared to hyperthyroid group and control group. Serum concentration of HDL-C increased after treatment of hyperthyroidism compared to the controls and hyperthyroid subjects[3]. Treatment of hyperthyroidism slightly increased the HDL-C[20].

## CONCLUSION

Our study confirmed the opposite effects of hyperthyroidism and hypothyroidism on HDL-C. HDL-C levels are decreased in hyperthyroid and increased in hypothyroid. HDL-C concentration in different thyroid disease states is still controversial. Treatment of both diseased states altered the levels of thyroid hormones and HDL-C. HDL-C was decreased in both treated groups. Treatment of thyroid can improve the abnormalities in lipid profile.

## REFERENCES

1. Benvenga S, Robbins J. Thyroid hormone efflux from monolayer cultures of human fibroblasts and hepatocytes. Effect of lipoproteins and other thyroxine transport proteins.Endocrinology 1998; 139: 4311-4318.
2. Gali R M, Gadaka M A, Mshelia D S, Gali B M, Okon K. Lipid profile pattern in thyroid disorders in northeastern Nigeria. Highland Med Res J 2007; 5: 20-26.
3. O'Brien T, Katz K, Hodge D, Nguyen T T, Kottke B A, Hay I D. The effect of treatment of hypothyroidism and

hyperthyroidism on plasma lipids and apolipoproteins AI, AII and E. ClinEndocrinol (Oxf ) 1997; 46: 17-20.
4. Diekman MJM, Anghelescu N, Endert E, Bakker O, Wiersinga WM. Changes in plasma low-density lipoprotein cholesterol in hypo- and hyperthyroid patients are related to changes in free thyroxine, not to polymorphisms in LDL receptor or cholesterol ester transfer protein genes. J Clinical EndocrinolMetab 2000; 85:1857-1862
5. Muls E, Rosseneu M, Bury J, Stul M, Lamberigts G, De-Moor P. Hyperthyroidism influences the distribution and apolipoprotein a composition of the high density lipoproteins in man. J ClinEndocrinolMetab 1985a; 61: 882-889.
6. Liberopoulos EN, Elisaf MS. Dyslipidemia in patients with thyroid disorders. Hormones (Athens) 2002; 1: 218-23.
7. Mansourian AZ, Ghaemi E, Ahmadi AZ, Marjani AJ, Akhtar SA, Bakhshandehnosrat S. Serum lipid level alterations in subclinical hypothyroid patients in Gorgan South East of Caspian Sea. J Chinese Clinicl Med2008;3:206-210.
8. Martha F, Edmundo C, Oscar PM. Pleiotropic effects of thyroid hormones: learning from hypothyroidism. J Thyroid Res 2011; 2011: 17.
9. Sigal GA, Mederiros-Neto G, Vinagre JC, Diament J, Maranhao RC. Lipid metabolism in subclinical hypothyroidism: plasma kinetics of triglyceride-rich lipoproteins and lipid transfers to high density lipoprotein before and after levothyroxine treatment. Thyroid 2011; 21: 347-353.
10. Tan KCB, Shiu SWM, Kung AWC**.** Effect of thyroid dysfunction on high-density lipoprotein subfraction metabolism: Roles of hepatic lipase and cholesteryl ester transfer protein. J ClinEndocrinolMetab 1998b; 83:2921-2924.
11. Heimberg M, Olubadewo JO, Wilcox HG. Plasma lipoproteins and regulation of hepatic metabolism of fatty acids in altered thyroid states. Endocrinol Rev 1985; 6: 590-607.
12. Caron p, Calazel C, Parra HJ, Hoff M, Louvet JP. Decreased HDL cholesterol in subclinical hypothyroidism: the effect of L-thyroxine therapy. ClinEndocrinol (Oxf) 1990; 33: 519-523
13. Efstathiadou Z, Bitsis S, Milionis HJ, Kukuvitis A, Bairaktari E, Elisaf M, et al. Lipid profile in subclinical hypothyroidism: is L-thyroxine substitution beneficial? Eur J Endocrinol 2001; 145: 705-710.
14. Fong BS, Greco AV, Angel A. Hypothyroidism reduces HDL binding to rat liver cells. Atherosclerosis 1989; 79: 1-8.
15. Muls E, Blaton V, Rosseneu M, Lesaffre E, Lamberigts G, De-Moor P. Serum lipids and apolipoproteins A-I, A-II, and B in hyperthyroidism before and after treatment.JClinEndocrinolMetab 1982; 55: 459-464.
16. Arieh R, Bianca R, Valentina B, Itzhack B, Baruch L, Ilana B. The influence of thyroid function on serum lipid profile. Atherosclerosis 1982; 41: 321-326.
17. Valdemarsson S, Hedner P, Nisson-Ehle P. Treatment of hyperthyroidism: Effects on hepatic lipase, lipoprotein lipase, LCAT and plasma lipoproteins. Scand J lab Invest 1984; 44: 183-189.
18. Verdugo C, Perrot G, Ponsin G et al. Time course of alteration of high density lipoproteins (HDL) during thyroxine administration to hypothyroid women. Eur J Clin Invest 1987; 17:313-316.
19. Friis T, Pedersen LR. Serum lipids in hyper- and hypothyroidism before and after treatment. ClinChimActa 1987; 62: 155-163.
20. Sucic M, Bozikov V, Mesic R, Sokolic L. Lipoprotein (a) levels in thyroid dysfunction before and after treatment. Croat Med J 1998; 39: 19-22.