Alterations in Lipid Profile in Old Age Hypothyroid Patients

S JAWED T F. KHAWAJA M. A SULTAN *T MAHMOOD*
Department of Physiology/Biochemistry, PGMI / SIMS / INMOL, Lahore
Correspondence to Dr. Samia Jawed, Assistant Professor

The current investigation was designed to study the changes of lipid profile in hypothyroid patients in local population a nd t o i nvestigate t he i mportance o f t hyroid p rofile i n o ld a ge d yslipidemia p atients. N inety f ive newly d iagnosed u ntreated h ypothyroid p atients (aged 4 9.21±12.47 y ears, BMI 3 0.36±5.8, 7 4 females a nd 2 1 males) were identified from thyroid OPD of INMOL, PGMI, Lahore. Patients were compared with 78 control subjects (aged 48.80±11.00 years, BMI 30.51±04.70, 54 females and 24 males) matched by age and body mass index (BMI). Serum TSH, FT4, FT3, Triacylglcerol (TAG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C) and high density lipoprotein cholesterol (HDL-C) were measured. Significantly increased levels of TC and LDL-C in overt hypothyroid patients were observed. No significant differences were found in HDL-C and TAG in overt hypothyroid patients as compared to the control group. Elevated levels of TC and LDL-C in hypothyroid patients represent an increased risk of ischaemic heart disease that requires therapeutic intervention. The deranged lipid profiles in hypothyroidism can not be corrected without the treatment for hypothyroidism in these patients. Therefore, all older patients referred for diagnosis and treatment of dyslipidemia should also be screened for hypothyroidism.
Key words: Lipid profile, hypothyroid, old age

Disorders of the thyroid gland, including hypothyroidism, are most common of all endocrine diseases with the exception of diabetes mellitus[1]. Overt hypothyroidism is associated with a bnormalities o f l ipid metabolism, which may predispose to the development of atherosclerotic coronary artery disease (CAD)[2-3]. The dyslipidemia is characterized by elevated levels of total and LDL-cholesterol which may be a consequence of decreased uptake of LDL-Cholesterol by its receptors on liver cell surfaces[4-5]. Because of marked prevalence of thyroid function abnormalities in the community[2,6-8], effects of thyroid hormones on lipid metabolism[9] and the well-defined role of circulating lipid concentrations in determining cardiovascular risk[10-11], it is important to investigate the alteration in circulating lipid levels in hypotl1yroid patients in our local population. It would also be pertinent to explore the significance of thyroid profile in dyslipidemic patients.

Subjects: All p atients were newly d iagnosed, u ntreated, and selected from thyroid OPD of INMOL. Ninety-five subjects (74 females and 21 males) aged 49.21±12.47 years with overt hypothyroidism were studied (TSH > 50 RIU/mil. The mean body mass index (BMT) of the patients wasd 30.36±5.80. Biochemical and clinical examinations were performed and a questionnaire was also filled in. by all subjects. Out of the 74 overt hypothyroid female studied, 49 were postmenopausal but none was receiving hormone replacement therapy at the time of study. Seventy-eight age and BMI matched healthy individuals 54 females (35 postmenopausal) and 24 m ale were included as the control group. The mean age of the controls was 48.80±11.00 years and mean BMI was 30.51±4.7.

All participants were excluded for smoking, diabetes mellitus, cardiac, renal, liver disease or familial hypercholesterolemia. Subjects receiving cholesterol-lowering drugs were also excluded from the study.

Methods: Blood samples were collected after overnight fasting of 12-14 hours. Serum was separated and stored at -20°C until analysed.

Free T4 (normal range 0.89-1.79 ng/dl) and free T3 (normal range 1.63 - 3.77 pg/ml) and TSH (normal range 0.17 - 4.05 mIU/L) were measured by radioimmunoassay using kits provided by (Immunotech, France). Radioactivity was measured on Gamma counter (Capintec, USA). The sensitivities of the assay were calculated to be 0.03ng/dl, 0.3pg/ml and 0.025mIU/L, for FT4, FT3 and TSH, respectively.

Serum total cholesterol (normal range <200 mg/dl) and HDL-cholesterol were measured by CHOD - PAP method. HDL-cholesterol was determined in the supernatant after precipitation with phosphotungstic acid and magnesium chloride (precipitating reagent). Triacylglecerol was measured by GPO enzymatic method (normal range <150 mg/dl). LDL-cholesterol was calculated using the Friedewald's formula (Friedewald *et al.*, 1972). All kits for lipid profile were supplied by Merck (Germany).

Statistical analysis: The results are expressed as mean±SEM and statistical difference was determined by employing Student's t-test.

Results:

The results of FT4, FT3, and TSH assays are shown in Table 1. R esults a re given a s mean ± S EM. S erum T SH levels were >50 mIU/ml (50 mIU/ml was the end detection Ihnit of the kit) in hypothyroid patients. The FT4 levels

were low in hypothyroid patients as compared to controls ($p<0.005$). Serum FT3 levels were within the reference range in hypothyroid patients.

The results of lipids and lipoprotein estimations in patients and controls are also shown in Table I and Figure 1. Alterations in parameters of lipid profile are expressed as % change form respective values of the normal subjects. Patients with overt hypothyroid had significantly higher serum levels of TC and LDL-C as compared to controls ($p<0.005$). No significant differences were observed in the serum levels of TAG and HDL-C, in hypothyroid patients and control subjects.

Table 1. Comparison of thyroid & lipid parameters in patients with overt hypothyroidism and control subjects

Paremeters	Overt hypothyroid (n=95)	Control (n=78)
TSH (mlU/ml)	> 50	2.83±1.31
FT4 (ng/dl)	0.21 ± 0.06*	1.45±0.22
FT3 (pg/dl)	1.92±0.15	2.49±0.83
TC (mg/dl)	240±9 15,<8	185±15.81
LDL-C (mg/dl)	160±10.34**	125±5.87
HDL-C (mg/dl)	35±3.84	39±4.31
TAG (mg/dl)	146±13.44	139±9.98

*p < 0.001**p< 0.005, respectively, when hypothyroid patients compared with control subjects. N.S: Non-Significant.

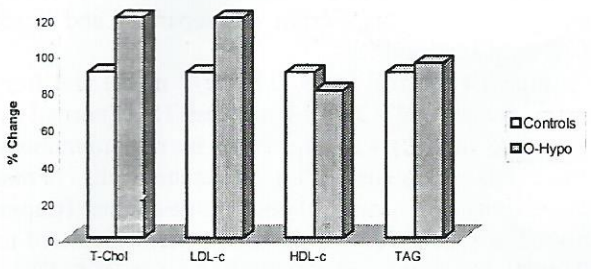

Fig.1: Comparison of serum lipid profile in control and patients with overt hypothyroidism

The values are expressed as percent change from the respective mean value of the same parameter for the controls. O-Hypo: Overt Hypothyroid Patients; T-Chol: Total Cholesterol; LDL-C; Low density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; TAG: Triacylglycerol

Discussion:

It is well known that thyroid dysfunction leads to changes in lipoprotein metabolism. Low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C) levels in blood are known to be increased hypothyroidism and decreased in hyperthyrodism[13-16]. The clearance of chylomicron remnants is decreased in hypothyroidism[17]. Changes in LDL-C are mainly attributable to altered clearance of LDL-C from plasma by changes in the number of LDL receptors on liver cell surfaces[18-19]. Because the promoter of the LDL receptor gene contains a thyroid hormone responsive element (TRE), T3 could modulate gene expression of the LDL receptor[20]. HDL-C metabolism is complex, and changes in plasma levels are due, in part, to remodeling of HDLC particles by hepatic lipase and cholesterol ester transfer protein (CETP)=21. Activity of both enzymes decrease in hypothyroidism and increase in hyperthyroidism correlating with plasma HDL-C[22-24]. Many previous studies have found that individuals with overt hypothyroidism have elevated total cholesterol and LDL-C levels[25-27].

Results of the current study showed significantly high levels of total cholesterol and LDL-C in hypothyroid patients as compared with normal control group. TAG and HDL-C levels, on the other hand, remained unaltered.

Conflicting results have been reported in several cross sectional studies of thyroid dysfunction and HDL-C levels. Compared with individuals with normal thyroid function, HDL-C has been reported to be high[14,28-29], low[30-32] or unchanged[27,33-35]. In a population based study it has been found that older women with elevated LDL-C were 80% more likely to have an elevated TSH, and those with abnormal levels of total cholesterol, LDL-C, and HDL-C were 90% more likely to have high TSH. Women with normal lipids levels were much less likely to have an elevated TSH[31].

The incidence of hypothyroid-ism in the population is age and sex related being commoner in women and in older age group[27-28]. On the basis of the results of the current investigation, along with others reported elsewhere, it is recommended that in patients with altered lipid profile, especially in older females, investigations of thyroid assay should be performed for proper diagnosis and treatment of hyperlipidemia.

References:

1. Hay ID. Klee GG. Thyroid dysfunction. Endocrinol Metab Clin North Anl 1988 17: 473-509.
2. Tunbridge WMG, Evered DC, Hall R, Appleton D, Bremis M, Clark F, Evans J G, Young E, Bird T and Smith PA. The spectrum of thyroid disease in a community: The Whickham survey. Clin Endocrinol 1988; 7: 481 -93.
3. Pucci E. Chiovato L, Pinchera A. Thyroid and lipid metabolism. Inter J Obes 2000; 24(suppl 2):S109-S112.
4. Abrams J, Grundy S. Cholesterol metabolism in hypothyroidism and hyperthyroidism in man J Lipid Res 1988; 22: 323-8.
5. Kovanen PT. Regulation of plasma cholesterol by hepatic low-density lipoprotein receptors. Anl Heart J 1987: 113: 464-69.
6. Parley JV, Franklyn JA, Cross KW, Jones SC, Sheppard MC. Prevalence and tollow-up of abnormal thyrotropin (TSH) concentrations in the elderly in the United Kingdom. Clin Endocrinol 1991; 34: 77-83.
7. Hollowell JG, Staehling NW, Flanders WD. Serum- TSH, T4 and thyroid antibodies in the United . States population (1988 to 1994): National Health and Nutrition Examination

Survey (NHANES III). J Clin Endocrinol Metab 2002; 87: 489-99.
8. Kanaya M A, H aris F , V olpato S , P erezstable J E, H aris T, Baver CD. .Association between thyroid dysfunction and total cholesterol level in an older biracial population.. Arch Intern Med 2001; 162:773-79.
9. Thompson GR, Soutar AK, Spengel FA. Detects of receptor mediated low density lipoprotein catabolism in homozygous tamilial hypercholes-terolaemia and hypothyroidism in vivo. Proc Natl Acad Sci USA 1981; 78: 2591-95.
10. Castelli WP. Epidemiology of coronary heart disease: the Framifigharn study. Am J Med 1984: 76 (Suppl.2a): 4-12.
11. National Cl1olesterol Education Program. Second report of the expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel IIf). Circulatios1 1988; 89:1333- 1445.
12. Friedewald WT. Levy RI, Fredrikson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma without use o f t he p reparative u ltracentrifuge. C lin Chem 1992; 18: 499-509.
13. Heimberg M, Olubadewo JO and Wilcox HG. Plasma lipoproteins and regulation of hepatic metabolism of fatty acid in altered thyroid states. Endocrine Rev 1985; 6: 590-615.
14. Muls E, Blaton V, Rosseneu M, Lesaffre E, Lamberigts G, De Moor P . Serum lipids and apolipoproteins A-I, A-II. J Clin Endocrinol Metab 1992; 55: 459-64.
15. Muls E, Rosseneu M, Blaton V, Lesaffre E, Lamberigts G, De Moor P. Serum lipids and apolipoproteins A-I, A-II, and B in primary hypothryroidism before and during treatment. Eur J Clin Invest 1984; 14:]2-15.
16. Diekman MJM, Anghlescu N, Endert E, Bakker O, Wiersinga MW. Clin Endocrinol Metab 2003; 85:1057-62.
17. Weintraub M, Grosskopf I, Trostaneky Y, Charach G, Rubinstein A, Stern N. Thyroxine replacement therapy enhances clearance of chylomicron remnants in patients with hypothyroidism. J Clin Endocrinol Metab 1999; 84: 2532-36.
18. Chait sBierman El, Albers JJ. Regulatory role of triiodothydronine in the degradation of low density lipoprotein by cultured human skin fibroablasts. J Clin Endocrinol Metab 1979; 48 887-89.
19. Souter AK, Knight BL. Structure and regulation of the LDL receptor and its gene. BrMed Bull 1990; 46: 891-916.
20. Bakker O, Huding F, Meijssen S, Wiersinga WM. Effects of triiodothyronine and amiodarone on the promoter of the human LDL receptor gene. Biochem Biophys Res Commun. 1998; 249: 517-21.
21. Tall AR. Plasma cholesterol transfer protein. J Lipid Res 1993; 34: 1255-74.
22. Dullaart RPF, Hoogenberg K, Groener JEM, Dikkeshei LD, Efkelens DW, Doorenbos H. The activity of cholesteryl ester transter protein is decreased in hypothyroidism: Eur J Clin Invest 1992; 20: 581-87.
23. Kitter MC, Kannan CR, Bagdade JD. The effects of hypothyroidism and replacement therapy on cholesteryl ester transfer. J Clin Endocrinol Metab 1996; 81: 797-800.
24. Tan KC, Shiu SW, Kung AW. Effect of thyroid dysfunction on high-density lipoprotein subfi-action metabolism: J Clin Endocl-inol Metab 2000; 83: 2921-24.
25. Sawin C,Geller A, Hershamtn J, Castelli W and Bacharach P. EChe aging thyroid. The use of thyroid holmone in older persons. J AM1 Med As.soc 1989; 261: 2653-55.
26. Stone NJ. Secondary causes of hyperlipidemia. Med Clin North Am 1994; 78: 117-41.
27. O'Brlen T, Dinneen SF, O' Brien PC, Palumbo PJ. Hyperlipidemia in patients with primary and secondary hypothyroidism. Mayo Clin Proc 1993; 68: 860-66.
28. Ball MJ, Griffiths D, Thorogood M. Asymptomatic hypothyroidism and hypercholesterolemia. J R Soc Med 1991; 84: 527-29.
29. Aviram M, Luboshitzky RR, Brook J. Lipid and lipoprotein pattern in thyroid dysfunction and the effect of therapy: Clin Biochem 1982; 15: 62-6.
30. Caron P, Calazel C, Parra HJ, Hoff M & Louvet JP. Decreased HDL cholesterol in subclinical hypothyroidism: The effect of L-thyroxine therapy. Clin Endocrin 1990: 33: 519-23.
31. Bauer CD, Ettinger B & Browner WS. Thyroid function and serum Lipids in older women: a population-based study. Am J Med 1998; 104: 546-51.
32. Agdeppa D, Macaron C, Mallik T, Schnuda ND. Plasma high-density lipoprotein cholesterol in thyroid disease. J Clin Endocrinol Metab 1989; 29; 49: 726-29.
33. Staub JJ, Althaus BU. Engler H. Am J Med 1992; 92: 631-41.
34. Bogner U, Arntz HR, Peters H, and Schleusener H. Subclinical h ypothyroidism a nd h yperlip o protein a em i a: Indiscriminate L-thyroxine treatment not justified. Acta Endocrinologica 1993; 128: 202-06.
35. Althaus BU, Staub JJ, Ryff:de Leche A. Clin Endocrin 1998; 28: 15763..