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# TO EVALUATE THE LIPID PROFILE OF PATIENTS WITH HYPOTHYROIDISM

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## ABSTRACT

This study aim at studying the lipid profile abnormalities in patients with hypothyroidism and its interpretation. The entire work has been carried out in the department of Biochemistry, Katihar Medical College & Hospital, Bihar, during the period from Dec' 2009 to May 2011. In the present case-control study patients were diagnosed as hypothyroid clinically from patients attending the Medicine out-patient department of Katihar Medical College & Hospital,Bihar. The entire study was conducted to establish a relationship between hypothyroidism and lipid profile status among the patients. Study included 100 cases and 100 controls. All cases had TSH level > 7.0 µIU/ml. Age and sex-matched controls were selected by simple random method among euthyroid persons and it was assured that selected controls are not suffering from any endocrine or metabolic disorders.The prevalence of hypothyroidism is higher among middle aged women. These results shows that the effect of hypothyroidism on Lipid profile is more marked in cases with higher serum TSH level. The level of TSH was expectedly high among the subjects with hypothyroidism. The level of TOTAL.CHOL was highly increased in patients of hypothyroidism. The mean value of serum triglyceride in subjects with normal thyroid function was 137.700 ± 1.85 mg/dl. The levels were significantly increased and went up to 295.67 ± 11.37mg/dl among the subjects with the hypothyroidisms. This was statistically significant as compared to controls with a p-value < 0.0000001.

**Keywords:** Thyroid, hypothyroid, dyslipidemia, subclinical thyroid, metabolic, cholesterol, free $T_3$, $T_4$, Lipoprotein, Ldl, Hdl, Vldl,

## INTRODUCTION

Hypothyroidism is defined as a deficiency of thyroid activity resulting from reduced secretion of both $T_3$ & $T_4$ (Seely and Williams, 2001). Biochemical decrease in T3 & T4 concentrations lead to hyper secretion of pituitary thyroid stimulating hormone (TSH) & which increases serum TSH level.

Hypothyroidism is more common in women particularly in reproductive age group (mainly in pregnancy) than in men (Sawin, Iunbridge, 1985 and Danse, 2000) and younger individuals. Thyroid disease is associated with various metabolic abnormalities, due to the effects of thyroid hormones on nearly all major metabolic pathways. Thyroid hormones regulate the basal energy expenditure through their effect on protein, carbohydrate and lipid metabolism. This might be a direct effect or an indirect effect by modification of other regulatory hormones such as insulin or catecholamine (Kim, 2008).

There are several known mechanisms for the observed effect of thyroid status on lipid concentration (Galesanu *et.al.,* 2004). In overt hypothyroidism, lipid synthesis & mobilisation, metabolism are severely affected (Duntas, 2002, Heimberg, 1985 and Cappola, 2003), moreover the composition & transport of lipoproteins are seriously disturbed in thyroid disease. Overt hypothyroid is associated with hypercholesterolemia & hypertriglyceridemia (Canaris, 2000 and Galesanu *et.al.,* 2002). It is also characterized by marked increased in circulating concentration of total cholesterol & low density lipoprotein (LDL-C) (Elder et.al., 1990, Staub *et.al.*, 1999 and Brien et.al., 1993) and apolipoproteion B(ApoB) because of decreased fractional clearance of LDL by a reduced number of LDL-receptor in the liver (Pearce, 2004 and Duntas, 2002). The high density lipoprotein (HDL) level is normal or even elevated in severe hypothyroidism (Agdeppa et.al., 1979, Aviram, 1982 and Lithell et.al., 1981) because of decreased activity of cholesteryl-ester transfer protein (CETP) which transfers cholesterol from HDL-Cholesterol to LDL-Cholesterol & very low density lipoprotein (VLDL-Cholesterol) & are regulated by thyroid hormone (Tan et.al., 1998). Thyroid hormone also appears to regulate hepatic lipase (HL), which alters HDL-Cholesterol sub-fraction & lowers serum triglyceride (TG) levels through hydrolysis of lipoproteins & facilitation of transfer of cholesterol from these lipoprotein to HDL-Cholesterol (Lam et.al., 1986). The low activity of CETP & more specifically of HL, results in reduced transport of cholesteryl ester from

$HDL_2$ to VLDL & intermediate density lipoprotein (IDL) & reduced transport of $HDL_2$ to $HDL_3$ (Duntas, 2002, Tan *et.al.,* 1998 and Pazos *et.al.,* 1995). Hypothyroidism increases the oxidation of plasma cholesterol mainly because of an altered pattern of binding & to the increased levels of cholesterol, which present a substrate for the oxidative stress (Biondi *et.al.,* 2002 and Nyirenda *et.al.,* 2005) & leads to atherosclerosis & coronary heart diseases (Rodondi *etal.,* 2006, Volzke *et.al.,* 2007, Singh *et.al.,* and Althaus *et.al.).*

Dyslipidaemia is a common metabolic abnormality in patients with thyroid disease, either in the overt or subclinical forms of the disease, and constitutes the end result of the effect of thyroid hormones in all aspects of lipid metabolism leading to various quantitative and/or qualitative changes of triglycerides, phospholipids, cholesterol and other lipoproteins (Zhu, 2010).

In thyroid disease, dyslipidaemia and co-existing metabolic abnormalities, in combination with the thyroid hormone-induced hemodynamic alterations, explain the high risk for cardiovascular disease (Biondi, 2004, Biondi, 2010, Klein, 2001 and Fazio *et.al.*, 2004).

Thyroid dysfunction is a major public health problem among Indian population. Hence the study is aimed to find out the prevalence of thyroid dysfunction and to investigate the effect of it in serum lipids. Serum fT3, fT4, TSH, total cholesterol (TC), low density lipoprotein (LDL), high density lipoprotein (HDL) and triglycerides (TG) were measured using standardized assays.

## MATERIAL & METHODS

This study aim at studying the lipid profile abnormalities in patients with hypothyroidism and its interpretation. The entire work has been carried out in the department of Biochemistry, Katihar Medical College & Hospital, Bihar, during the period from Dec' 2009 to May 2011. In the present case-control study patients were diagnosed as hypothyroid clinically from patients attending the Medicine out-patient department of Katihar Medical College & Hospital, Bihar. Out of them, hundred hypothyroid patients were selected by simple random method. Age and sex-matched controls were selected by simple random method among euthyroid persons and it was assured that selected controls are not suffering from any endocrine or metabolic disorders. Written consents were taken from all cases & controls after informing them about the risks and benefits of this study. Blood was drawn from antecubital vein after overnight fasting from both the cases and controls. Serum was prepared and was made ready for measurement of following parameters

- Serum free $T_3$ ($fT_3$) and $T_4$ ($fT_4$) by competitive enzyme-linked immunosorbent assay (ELISA) method.
- Serum TSH by sand-witch ELISA method.
- Serum cholesterol by cholesterol oxidase-peroxidase (CHODPAP) method.
- Serum triglyceride by glycerol-3-phosphate oxidase (GPO) method.
- Serum VLDL value (in mg/dl) was calculated by dividing the value of TG by 5.
- Serum LDL value was calculated by Fried-Wald equation.
- Serum HDL value was assessed by precipitation method.

Reference Range of free T3 (fT3) by ELISA Method[42]
Adult - 1.4-4.2 pg/ml
Pregnancy - 1.8-4.2 pg/ml
Normal Range of free T4 (fT4) by ELISA Method-:[43]
Adult → 0.8-2.0ng/dl
Pregnancy → 0.76-2.24ng/dl

**NORMAL RANGE OF TSH[44]**
**ADULT - 0.39- 6.16 µ IU/ML**
**SERUM LIPID PROFILE INCLUDES-**

- Serum cholesterol
- Serum triglyceride
- Serum High density lipoprotein (HDL)
- Serum low density lipoprotein (LDL)
- Serum very low density lipoprotein (VLDL)

**SERUM TOTAL CHOLESTEROL ESTIMATION –**

**METHOD: CHOLESTEROL OXIDASE & PEROXIDASE (CHOD-PAP)**

**FOR HDL CHOLESTEROL**

LDL cholesterol, VLDL and chylomicron fraction are precipitated by addition of Polyethylene Glycol 6000 (PEG.) After centrifugation, the HDL fraction remains in the supernatant and is determined with CHOD-PAP method.

**CALCULATION**
**FOR TOTAL CHOLESTEROL**

$$\text{Cholesterol concentration (mg/dl)} = \frac{\text{Absorbance of "unknown"}}{\text{Absorbance of "Standard"}} \times 200$$

**For HDL cholesterol**

$$\text{HDL-Cholesterol concentration (mg/dl)} = \frac{\text{Absorbance of "unknown"}}{\text{Absorbance of "Standard"}} \times 50X2^*$$

*(2= Dilution factor, as sample was diluted 1:1)

**For LDL cholesterol using Friedwald's equation****

$$\text{LDL – cholesterol} = \frac{\text{Total cholesterol – Triglyceride – HDL cholesterol}}{5}$$

** Friedwald equation is unsuitable when:

- Sample has high concentration of triglyceride ie. >400mg/dl and contains significant of chylomicrons (non-fasting sample)
- Type III hyperlipoproteinaemia, a rare but severe disorder.

**Reference range** (Jackson, 1982 and Li et.al., 1990)

| Remarks | Total cholesterol concentration in serum (Mg/dl) |
|---|---|
| Desirable | <200 |
| Borderline high | 200-239 |
| High risk | ≥ 240 |

| Remarks | HDLs concentration in serum (mg/dl) |
|---|---|
| Low risk | ≥ 60 |
| High risk | ≤ 40 |

**TRIGLYCERIDE**

**Method: Glycerol -3- phosphatc oxidase & peroxidase method (GPOPAP)**

**Calculation**

$$\text{Triglyceride concentration (mg/dl)} = \frac{\text{Absorbance of "unknown"}}{\text{Absorbance of "Standard"}} \times 200$$

**REFERENCE RANGE (Li et.al., 1990)**

| Remarks | Triglyceride concentration in mg/dl |
|---|---|
| Normal | < 150 |
| Borderline high | 150-199 |
| High | 200-499 |
| Very high | ≥ 500 |

**STATISTICAL ANALYSIS**

The data were fed in a computer and analysed using software SPSS 15.0 and Microsoft excel. Tests used: Chi-square test was applied for comparing qualitative data and independent t-test was applied for comparing quantitative data.

**DISCUSSION**

The entire study was conducted to establish a relationship between hypothyroidism and lipid profile status among the patients. This was a case control study done over a period from December 2009 – May 2011. Study included 100 cases and 100 controls. All cases had TSH level > 7.0 µIU/ml. The data presented in this study in the form of mean ± standard error of mean (S.E.M.).

All controls had normal thyroid profiles. Age & sex matched controls were taken. Mean age of patients of hypothyroidism 34.81 ± .949 years. Mean age of Controls group is 30.96 ± .859 years. This was similar to study by Sanjoy K Bhandopadyay *et al*[47] where it was 38.56 years. This finding is statistically significant with p-value is less than 0.001. More number of cases was seen between 18 to 35 years age group.

This study showed female predominance with 85%. Only 15% of total study population was males. This was similar to the study by Sanjoy K Bhandopadyay et all[47] where females constituted 78% of study populations. Many major studies have been done only on women. Cases had a mean total fT3 value of 2.187 ± .0919pg /ml. fT3 levels between cases & controls were almost statistically similar. This is an expected finding because; peripheral deiodination of T4 to T3 is unaffected in subclinical hypothyroidism. Study by Salmon Rizvi et al has yielded similar results. P-value of fT3 was 0.268940 so the difference between cases and control was statistically not significant. This may be due to subjects of hypothyroidism were taken L-thyroxin. A mean fT4 level among patients of hypothyroidism was 0.9387 ± 0.366ng/dl while the levels of fT4 among normal subject were 1.190 ± 0.034366ng/dl. This increased value of fT4 among subjects was statically significant with p-value < 0.00001. fT4 levels in cases were towards the lower limit of normal range.

This was similar to a study by Krishnaveni. D.V in her study the mean value of total T4 was 2.73 ± 1.88 µg/dl as compared to their control group where it was 7.75 ± 1.72µg /dl. The changes were statistically significant with p-value less than 0.001.

In present study shows mean TSH values of cases was 30.96 ± 2.082µIU/ml while the value among control was remained 1.832±0.0923µIU/ml.

Mean value of Total cholesterol among the subjects of hypothyroidism was 326 ± 6.339 mg/dl . This was highly increased to the normal levels and the elevation of Total cholesterol was statistically highly significant when compared with their normal counterparts with p value< 0.000001.

This study is similar to the study by Krishnaveni. D. V[48] in her study Total Cholesterol level in cases of hypothyroidism was 266.50 ± 47.60 in mg% when compared to controls and in this group level of Total Cholesterol was 175 ± 17.62 in mg%. This was very significant statistically with P-value was less than 0.0001.

Efstathiadou et al[49] found a mean total cholesterol value of 222 mg/dl. William J. Hueston et al demonstrated total cholesterol level of 217mg/dl.

Mean HDL-cholesterol levels in hypothyroid patients was 53.15 ± 1.079 mg/dl. While the level of HDL-Cholesterol among control group had 42±.761mg/dl. This increase in HDL-Cholesterol was significant when compared with the normal subjects with p-value less than 0.001.

Heimberg M. et. al., found that hypothyroid patients usually exhibits elevated levels of HDL-Cholesterol mainly due to increased concentration of HDL-2 particles (Heimberg, 1985). In another study it was found that the decreased Activity of CETP results in reduced transfer of cholesteryl ester from HDL-Cholesterol to VLDL-Cholesterol, thus increasing HDL-Cholesterol level (Lachlan, 1992).

Kong et al (1988) have shown mean HDL-cholesterol value was 39 mg/dl. Rajan et al (1995) have shown HDL value of 41.5mg/dl which was not statistically significant.

The mean value of serum triglyceride in subjects with normal thyroid function was 137.700 ± 1.85 mg/dl. The levels were significantly increased and went up to 295.67 ± 11.37mg/dl among the subjects with the hypothyroidisms. This was statistically significant as compared to controls with a p-value < 0.0000001. In patients of hypothyroidism activity of lipoprotein lipase in adipose tissue has been found normal or decreased, in addition to decreased hepatic lipase activity resulting in normal or high levels of triglycerides (Abrams et.al., 1981,

Lam et.al., 1986 and Krauss et.al, 1974). In different study Kong et al[53] reported mean value of triglyceride was159mg/dl. And William J. Hueston et al (1985) have shown mean triglyceride value of 178.1mg/dl in their study. The value of LDL-Cholesterol was higher among the subjects with hypothyroidism as compared to control groups. Control group had mean LDL-cholesterol level was 66.60 ± 5.49mg/dl which was elevated up to 215.17 ± 5.49 in the cases of hypothyroidism. This increase in LDL-Cholesterol level was highly significant statistically with p- value of 0.0000001. This finding is similar to the study done by Krishnaveni.D. V in her study level of LDL-cholesterol in cases of hypothyroid patient was 203.76 ± 50.11 in mg% as compared to control group which was 118.23 ± 15.46 mg%. This was very significant statistically with p-value was less than 0.00001.

Rajan et.al[52] have shown mean LDL value of 134mg/dl with statistical significance. Tromso study (Geul, 1993) also demonstrated elevated LDL-cholesterol levels which came down after treatment. In Present study the value of VLDL-Cholesterol in subject without hypothyroidism was 29.28 ± 0.397 which were significantly increased to 59.074 ± 2.282 mg/dl in case of subjects with hypothyroidism with p-value of 0.00001. Krishnaveni. D.V. done a study on hypothyroid patients and in her study value of VLDL-cholesterol was statistically significant. Hypertriglyceridemia associated with increased levels of VLDL and occasionally fasting chylomicronemia are found less commonly in hypothyroidism these changes are attributable to the decreased activity of LPL, which results in a decreased clearance of triglyceride-rich lipoproteins (Miura et.al., 1994 and Korbonits, 1998).

The prevalence of hypothyroidism is higher among middle aged women. These results shows that the effect of hypothyroidism on Lipid profile is more marked in cases with higher serum TSH level.

## SALIENT FINDINGS

1. The level of fT3, fT4, TSH is normal in all control groups.
2. The level of fT3 and fT4 was within the normal limit in the study group, the mean value of fT4 falling in the lower limit of normal range.
3. The level of TSH was expectedly high among the subjects with hypothyroidism.
4. The level of TOTAL.CHOL was highly increased in patients of hypothyroidism.
5. The level of HDL-CHOL was increased in the subjects of hypothyroidism when compared with controls.
6. The TRIGLYCERIDE level was increased in the subjects of hypothyroidism.
7. The level of VLDL-CHOL was increased in the subjects of hypothyroidism.
8. The level of LDL-CHOL was increased in the subjects of hypothyroidism.

## REFERENCES


- Agdeppa D, Macaron C, Mallik T, Schnuda ND. Plasma high density lipoprotein cholesterol in thyroid disease. J Clin Endocrinol Metab, 1 979;49 :726-729.
- Althaus BU, Staub JJ, Ryff-De Leche A, Oberhansli A, Stahelin HB. LDL/HDL – chages in subclinical ein. Hypothyroidism: possible risk factors for coronary heart disease. Clin Endocrinol (Oxf). 1
- Aviram M, Luboshitzky R, Brook JO. Lipid and lipoprotein pattern in thyroid dysfunction and the effect of therapy. Clin Biochem, 1982; 15:62-66.
- B. Biondi and G. J. Kahaly, “Cardiovascular involvement in patients with different causes of hyperthyroidism,” Nature Reviews Endocrinology, vol. 6, no. 8, pp. 431–443, 2010.
- B. Biondi and I. Klein, “Hypothyroidism as a risk factor for cardiovascular disease,” Endocrine, vol. 24, no. 1, pp. 1–13, 2004.
- B. Kim, “Thyroid hormone as a determinant of energy expenditure and the basal metabolic rate,” Thyroid, vol. 18, no. 2, pp. 141–144, 2008.
- biological activity. Thyroid; 1998:8; 941.
- Biondi B, Palmieri EA, Lombardi G, Fazio S. Effects of subclinical thyroid dysfunction on the heart. Ann Intern Med. 2002;137:904-914.
- Blenneman B, Leahy P, Kim TS, Freake HC. Tissue specific regulation of lipogenic mRNAs by thyroid hormone. Mol cell Endocrinol 1995: 110; 1.
- Boyd JD. Development of the human thyroid gland. In: Pitt-Rivers R, The Thyroid. Vol. 1.washington DC; Butterworth: 1964:9.
- Brien T, Dinneen SF,0 Brien PC, PalumboPJ.Hyperlipidemia in patients with primary and secondary hypo-thyroidism.Mayo Clinics Proceedings, 1993;68:860-866.
- Canaris GJ, Manowitz NR, Mayor U, Ridgway EC. The Colorado Thyroid Disease Prevalence Study. Arch Tnt Med. 2000;160:526-534.
- Cappola AR, Ladenson PW. Hypothyroidism and atherosclerosis. Journal of Clinical Endocrinology and Metabolism, 2003;88:2438- 2444.
- Caron P, Calazel C, Parra HJ et al: Decreased HDL-cholesterol in subclinical hypothyroidism. The effect of L-thyroxine therapy. Clin Endocrinol 1990; 33:519.
- Danse MD, Landenson PW, Meinert CM, and NR Powe. Effect of thyroxin therapy on serum lipoprotein in patients with mild thyroid failure: a quantitative review of the literature. J Clin Endocrinol Metab, 2000;85:2993-3001.
- Duntas LH. Thyroid disease and lipids. Thyroid. 2002; 12:287-293.
- Elder J, St McLelland AJ, 0 Reilly D, Packard CJ, series JJ, Shepherd J. The relationship between serum cholesterol and serum thyrotropin, thyroxin and tri-iodothryronin concentration in suspected hypothyroidism. Annals of Clinical Biochemistry,1990;27:l1O-113.

- Fisher DA, Polk DH. Development of the thyroid. Ballieres Clin Endocrinol Metab 1989; 3: 67.
- G. Sauter, M. Weiss, and R. Hoermann, "Cholesterol 7α-hydroxylase activity in hypothyroidism and hyperthyroidism in humans," Hormone and Metabolic Research, vol. 29, no. 4, pp. 176–179, 1997.
- Galesanu C, Lisnic N, Teslaru R, Apostu L, Zbranca E,. Lipids profile in a group of hypothyroid patients VS. treated hypothyroid patients. Rev Med Chir Soc Med Nat lasi. 2004;108(3):554-60.
- Geul KW, Grobbee DE et al. The importance of thyroid microsomal antibodies in the development of elevated serum TSH in middle aged women; association with serum lipids. Clin Endocrinol 1993; 39: 275.
- Heimberg M, Olubadewo JO, Wilcox HG. Plasma lipoproteins and regulation of hepatic metabolism of fatty acids in altered thyroid status. Endocrine Reviews, 1985 ;6 :590-607.
- J. A. Berti, M. E. C. Amaral, A. C. Boschero et al., "Thyroid hormone increases plasma cholesteryl ester transfer protein activity and plasma high-density lipoprotein removal rate in transgenic mice," Metabolism, vol. 50, no. 5, pp. 530–536, 2001.
- J. J. Abrams, S. M. Grundy, and H. Ginsberg, "Metabolism of plasma triglycerides in hypothyroidism and hyperthyroidism in man," Journal of Lipid Research, vol. 22, no. 2, pp. 307–322, 1981.
- Jackson IMD: Thyrotropin releasing hormone. N Engl J Med 1982:306:145
- K. S. L. Lam, M. K. Chan, and R. T. T. Yeung, "High-density lipoprotein cholesterol, hepatic lipase and lipoprotein lipase activities in thyroid dysfunction—effects of treatment," Quarterly Journal of Medicine, vol. 59, no. 229, pp. 513–521, 1986.
- Klein and K. Ojamaa, "Thyroid hormone and the cardiovascular system," The New England Journal of Medicine, vol. 344, no. 7, pp. 501–509, 2001.
- Korbonits M. leptin and the thyroid- a puzzle with missing pieces. Clini Endocrinol 1998; 49:569.
- Lam KS, Chan MK, Yeung RI. High density lipoprotein cholesterol, hepatic lipase and lipoprotein lipase activities in thyroid dysfunction: effect of treatment. QJ Med. 1986;59:5l3-521.
- Li S, Crenshaw EB: 3ed, Rawson EJ et al. Dwarf locus mutants lacking three pituitary cell types result from mutations in the POU domain gene pit-12. Nature 1990; 347:528.
- Lithell H, Boberg J, Hellsing K, Ljunghall 5, Lundqvist 0, Vessby B, Wide L. Serum lipoprotein and apolipoprotein concentration and tissue lipoprotein-lipase activity in overt and subclinical hypothyroidism: the effect of substitution therapy. Eur J Clin Invest. 1981;ll:3-1O.
- McLachlan SM, Rapaport B. the molecular biology of thyroid peroxicase: cloning, expression and role as autoantigen in autoimmune thyroid disease. Endocr Rev 1992: 13:192.
- Miura S, Iitaka M, Yoshimura H et al. Disturbed lipid metabolism in patients with subclinical hypothyroidism. Effect of L-thyroxine therapy. Intern Med 1994; 33:413.
- N. A. Cachefo, P. Boucher, C. Vidon, E. Dusserre, F. Diraison, and M. Beylot, "Hepatic lipogenesis and cholesterol synthesis in hyperthyroid patients," Journal of Clinical Endocrinology and Metabolism, vol. 86, no. 11, pp. 5353–5357, 2001.
- Nyirenda MJ, Clark DN, Finlayson AR, Read J, Elders A, Bain M, Fox KA, loft AD. Thyroid disease and increased cardiovascular risk. Thyroid. 2005;15:718-724.
- Parle JV, Franklyn JA, Cross KW, et al. Circulating lipids and minor abnormalities of thyroid function. Clin Endocrinol 1992; 37:411.
- Pazos F, Alvarez JJ, Rubies-Prat J, Varela C, Lasuncion MA. Long- term thyroid replacement therapy and levels of lipoprotein(a) and other lipoproteins. J Clin Endocrinol Metab. 1995;80:562-566.
- Pearce EN. Hypothyroidism and dyslipideniia: modern concepts and approaches. Curr Cardiol Rep. 2004;6:45 1-456.
- Persani L: Hypothalamic Thyrotropin releasing hormone and Thyrotropin
- R. M. Krauss, R. I. Levy, and D. S. Fredrickson, "Selective measurement of two lipase activities in postheparin plasma from normal subjects and patients with hyperlipoproteinemia," Journal of Clinical Investigation, vol. 54, no. 5, pp. 1107–1124, 1974.
- Robbins J: Thyroid hormone transport and metabolism: In Werner's & Ingbar's."The Thyroid". Eighth edition. Braverman LE, Utiger RD Lippincot 2000: 105-112.
- Rodondi N, Aujesky D, Vittinghoff E, Cornuz J, Bauer DC. Subclinical hypothyroidism and the risk of coronary heart diseases: a meta-analysis. Amj Med 2006;l 19:541-551.
- S. Fazio, E. A. Palmieri, G. Lombardi, and B. Biondi, "Effects of thyroid hormone on the cardiovascular system," Recent Progress in Hormone Research, vol. 59, pp. 31–50, 2004.
- Sawin CT, WP Castelli, JM Hershman, et. al. The aging thyroid, Iunbridge WMG, Evered DC, Hall R, et. al. The spectrum of thyroid disease in a community: the Whickham survey. Clin Endocrinol (Oxf), 1985;7:481-483.

- Sawin CT: The heritage of the thyroid. In Werner's & Ingbar's "The Thyroid". Eighth edition. Braverman LE, Utiger RD. Lippincot 2000.
- Seely EW, Williams GH, The heart in Endocrine Disorder In: Eugene Braunwald, Douglas P. Zipes ed. Heart Disease 6th edition. W.B. saunders Company, Philadelphia, 2001: 2151-2171.
- Singh S, Duggal J, Molnar J, Maldonado F, Barsano CP, Arora R, Impact of subclinical thyroid disorders on coronary heart disease, cardiovascular and all-cause mortality: a meta analysis. Int J Cardio,l, in press.
- Smith RB, McLachlan SM, Furmaniak J. Autoantibodies to the Thyrotropin receptor. Endocr rev 1988; 9:106.
- Staub JJ, Aithaus BU, Engler H, Ryff AS, Trabucco P, Marquardt K et.al. Spectrum of subclinical and overt hypothyroidism; effect on thyrotropin, prolactin, and thyroid reserve, and metabolic impact on perpheral target tissues. American Journal of Medicine, 1992;92:631- 642.
- Tan KCB, Shiu SWM, Kung AWC. Effect of thyroid dysfunction on high-density lipoproteion subfraction metabolism: roles of hepatic lipase and cholesteryl ester transfer prot J Clin Endocrinol Metab. 1998;83 :2921-2924.
- Tan KCB, Shiu SWM, Kung AWC. Plasma cholesteryl ester transfer protein activity in hyper- and hpothyroidism. J Clin Endocrinol Metab, l998;83:140-143.
- Tancevski, A. Wehinger, E. Demetz et al., "Reduced plasma high-density lipoprotein cholesterol in hyperthyroid mice coincides with decreased hepatic adenosine 5′-triphosphate-binding cassette transporter 1 expression," Endocrinology, vol. 149, no. 7, pp. 3708–3712, 2008.
- Tunbridge WMG, Evered DC, Hall R, et al. The spectrum of thyroid disease in a Community: the Whickham survey. Clin Endocrinol (Oxf) 1977; 7:481-493.
- V. A. B. Drover and L. B. Agellon, "Regulation of the human cholesterol 7α-hydroxylase gene (CYP7A1) by thyroid hormone in transgenic mice," Endocrinology, vol. 145, no. 2, pp. 574–581, 2004.
- Volzke H, Schwahn C, Wallachofski H, Doff M. The association thyroid dysfunction with all-cause and circulatory mortality: is there a causal relationship? J Clin Endocrinol Metab. 2007;92:2421-2429.
- X. Zhu and S. Y. Cheng, "New insights into regulation of lipid etabolism by thyroid hormone," Current Opinion in Endocrinology, Diabetes and Obesity, vol. 17, no. 5, pp. 408–413, 2010.
- Y. Y. Liu and G. A. Brent, "Thyroid hormone crosstalk with nuclear receptor signaling in metabolic regulation," Trends in Endocrinology and Metabolism, vol. 21, no. 3, pp. 166–173, 2010.