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**Research Article**

# ELEVATED RATIO OF VLDL/HDL IN HYPOTHYROIDISM MAY INDICATE FUTURE RISK OF RENAL DYSFUNCTION

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**ABSTRACT**

Hypothyroidism is characterized by hypercholesterolemia and hypertriglyceridemia. This deranged levels of lipid and lipoproteins over a long period of time may affect functioning of kidney by various mechanisms. Thus estimating levels of lipids and lipoproteins become an important diagnostic and prognostic tool.

**Material and methods:** The present cross sectional study included 30 clinically diagnosed and biochemically confirmed cases of hypothyroidism compared with 30 age and sex matched controls.

**Results:** It was observed that serum levels of triglycerides, Very low density lipoprotein were increased highly significantly ($P < 0.001$), while levels of HDL was decreased significantly ($P < 0.05$) in the experimental group as compared to control. The ratio of VLDL/HDL and TG/HDL were also increased highly significantly ($P < 0.001$) in the experimental group as compared to control.

**Conclusion:** Thus it can be concluded that elevated ratio of VLDL/HDL and in hypothyroidism may indicate future risk of renal dysfunction.



## INTRODUCTION

Dyslipidemia is characterized by abnormal levels of serum lipids. Circulating levels of high lipids or lipoproteins may contribute to various disorders. Elevated cholesterol is known to be predisposing factor of cardiovascular diseases. Elevated Similarly levels of lipoproteins may cause kidney damage by various ways. Firstly, circulating lipids bind to and become trapped by extracellular matrix molecules where they undergo oxidation. Macrophages phagocytise oxidized lipids and undergo transition to foam cells. Macrophage derived foam cells release cytokines thus recruiting more and more macrophages to the lesion. This influences lipid deposition, endothelial cell function and vascular smooth muscle cell (VSMC) proliferation. Eventually VSMC also become foam cells. This lipid mediated changes in the intrinsic kidney cells lead to glomerulosclerosis and interstitial fibrosis. Secondly, oxidized LDL is taken up by scavenger receptors (SR), including SR-A1 and CD36 (SR-BII). Acetylated and oxidized LDL bind to SR-A1 receptor and are endocytosed. Cholesteryl ester is hydrolysed in lysosomes to produce free cholesterol which can be toxic to cells[1] Oxidised low density lipoprotein (LDL) also up regulates CD 36 expression leading to progressive lipid accumulation thus accelerating vessel injury.[2]Very low density lipoprotein (VLDL) stimulates the expression of macrophage chemotactic protein-1 in mesangial cells.[3] It is chemotactic for macrophages which can infiltrate the glomerulous and become foam cells.[4] Lipids also contribute to renal disease through immune complex of oxidized LDL-antioxidised LDL[5]. HDL reduces oxidation of LDL and inhibit cytokine-induced expression of adhesion molecules on endothelial cells. HDL blocks the normal increase in CD36 thus decreasing CD36 mediated uptake of oxidized LDL[6]. This suggests that the elevated levels of cholesterol and triglycerides, lipoproteins like VLDL, LDL and decreased levels of HDL may contribute to renal dysfunction through various mechanisms. There are various conditions in which lipid profile is affected eg. Diabetes, Atherosclerosis etc. Hypothyroidism is one of them. Recent population-based study in India reported prevalence of hypothyroidism as 3.9%[7]. Thyroid hormones play important role in lipid metabolism. It inhibits LDL oxidation, upregulates LDL receptors which results in enhanced catabolism of LDL. Secondly it stimulates cholesteryl ester transfer protein (CETP) which transports cholesteryl ester from high density lipoprotein ($HDL^{-2}$) to VLDL and IDL and triglycerides in opposite direction. Thirdly it activates lipoprotein lipase (LPL) which hydrolyses TG rich lipoproteins. Fourthly it activates hepatic lipase which catabolises HDL2 to HDL3 and IDL to LDL. Lastly it inhibits LDL oxidation. Hypothyroidism is characterized by decreased levels of T3 and T4 and is commonly associated with hypercholesterolemia. Also alterations in composition of

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circulating triglycerides and decreased removal due to decreased activity of hepatic and lipoprotein lipase leads to hypertriglyceridemia. The present study was focused on estimation of very low-density lipoprotein, triglycerides, high-density lipoprotein cholesterol, and the ratios of TG/HDL and VLDL/HDL. Of these parameters, triglycerides and HDL are estimated by traditional methods while VLDL derived by Fredrickson- Friedewald Equation**.** The results were compared between cases and controls.

***Objectives***

To estimate the levels of TG, VLDL, HDL.
To estimate the ratio of TG/HDL
To find the ratio of VLDL/HDL

## MATERIAL AND METHODS

The present cross sectional study and has been carried out in the department of Biochemistry after approval by the Ethical Committee of the Institute.

***Inclusion and Exclusion criteria***

***Inclusion criteria:*** All newly diagnosed and untreated cases of hypothyroidism of both sexes of age group above 15 years who were willing to give consent were enrolled in study as cases.

***Controls:*** age and sex matched healthy individuals and those who were ready to give consent were selected as controls.

***Exclusion criteria:*** Patients suffering from diabetes mellitus, polycystic ovarian diseases, obesity tuberculosis, other systemic illness, liver disorders, renal disorder, and congestive cardiac failure, patients taking oral contraceptive pills, statins and other medications that alter thyroid function test were excluded. Patients already on treatment for hypothyroidism were also excluded from the study. All the study subjects above 15 years of age were examined & selected as per thyroid function tests. Total 60 samples were analyzed and were divided into two groups.

***Group A:*** (30) 30 age and sex matched euthyroid subjects with normal thyroid function test were enrolled in present study as control group.

***Group B:*** Consists of 30 clinically diagnosed and biochemically confirmed cases of hypothyroidism. These were selected from patients attending outpatient department of internal medicine, endocrine OPD and wards.

## METHOD

5 ml of 12 to 14 hours fasting venous sample was withdrawn after taking all aseptic precautions using sterile needles and syringes. Haemolysed, icteric and lipemic samples were excluded from the study. The blood sample was allowed to clot for 45 minutes in a clean dry sterile plain bulb. Thereafter the tube was centrifuged for 15 minutes at 2500 rpm to separate the serum. Serum was used for estimation of the thyroid function test[8, 9, 10,11]TG and HDL. The blood samples were analyzed immediately and those samples that were not processed immediately were capped and stored at - $20^0$ C until further analysis. TG[12] and HDL[13,14,15] were measured by enzymatic kit method, VLDL were estimated by Friedewald equation[16]. The results were analyzed statistically using SPSS software.

## RESULTS

The data obtained was compared between group A and group B. As shown in table 1 it was found that serum levels of TG and VLDL were increased highly significantly in group B as compared to group A ($P < 0.001$). While serum levels of HDL were decreased and this decrease is highly significant in group B as compared to group A ($P < 0.001$). The ratio of TG/HDL and VLDL/HDL were also increased highly significantly in group B as compared to group A ($P < 0.001$).

**Table 1** shows the levels of TG, VLDL, HDL and ratio of TG/HDL and VLDL/ HDL

| Parameters | GroupA(n=30) (mean± SD) | Group B (n=30) (mean ± SD) | P value |
|---|---|---|---|
| TG(mg/dl) | 129.2 ± 20.9 | 190.8 ± 17.1 | P < 0.001** |
| VLDL(mg/dl) | 25.85 ± 4.1 | 38.16 ± 3.4 | P < 0.001** |
| HDL (mg/dl) | 40.83 ± 3.4 | 38.96 ± 2.2 | P < 0.05* |
| TG/HDL | 3.19 ±0.6 | 4.91± 0.5 | P < 0.001** |
| VLDL/HDL | 0.64 ± 0.02 | 0.98 ± 0.02 | P < 0.001** |

(P < 0.05* significant, P < 0.001** highly significant)
Abbreviations:
TG = Triglycerides, VLDL= very low density lipoproteins, HDL= high density lipoproteins.

## DISCUSSION

Hypothyroidism is one of the most common disorders seen in present days. It is associated with hypertriglyceridemia along with hypercholesterolemia. In this study also the mean serum triglyceride levels in group B were significantly higher as compared to group A ($p<0.001$). Triglycerides are mainly transported as VLDL. So the levels of VLDL were calculated. It was observed that the mean serum VLDL levels of Group B were significantly higher as compared to group A ($P < 0.001$). It is known that hypertriglyceridemia is associated with increased levels of VLDL and chylomicron because of decreased activity of lipoprotein lipase which results in a decreased clearance of triglyceride rich lipoprotein in hypothyroidism. This is because thyroid hormones also play an important role in hydrolyzing triglyceride rich lipoproteins by activating lipoprotein lipase. Thus decreased lipoprotein lipase activity could prolong circulation time of VLDL. In this study the mean serum levels of protective lipoprotein HDL cholesterol were decreased significantly in group B as compared to group A ($p<0.05$). This could be because HDL particles associated with high triglyceride concentrations may be more readily catabolised[17,18]. High levels of triglycerides are often associated with low HDL cholesterol, especially in insulin-resistant individuals. Insulin resistance is frequently associated with hypothyroidism.[19]The ratio of TG / HDL indicator of presence of insulin resistance was calculated to know the load of TG and was found tobe increased highly significantly ($p<0.001$). It is reported in other studies that VLDL stimulates the expression of macrophage chemotactic protein-1 in mesangial cells.[3] It is chemotactic for macrophages which can infiltrate the glomerulous and become foam cells[4]that release cytokines and further modulate MC proliferation and matrix accumulation that perpetuate vascular injury. Thus VLDL has potential of affecting renal functions[2,3]. So to know the effective load of VLDL in presence of low HDL the ratio of VLDL/HDL was calculated. It was observed in the study that the ratio was increased highly significantly (p<

0.001) indicating that the ratio of VLDL/HDL can be used as a new marker to predict future risk of renal dysfunction.

Thus increased ratio VLDL / HDL indicates that the patients of hypothyroidism in this study may have future risk of renal dysfunction. Thus decreasing this ratio will help in monitoring the treatment of hypothyroidism and protecting individual from future risk of renal dysfunction.

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## References

1. Podrez EA, Febbraio M, Sheibani N, Schmitt D, Silverstein RL, Hajjar DP, Cohen PA, Frazier WA, Hoff HF, Hazen SL: Macrophage scavenger receptor for LDL modified by monocyte generated reactive nitrogen species. *J Clin Invest* 2000; 105: 1095-1108.
2. Han J, Hajjar DP, Tauras JM, Nicholson AC: Cellular cholesterol regulates expression of the macrophage type B scavenger receptor, CD36. *J Lipid Res* 1999; 40: 830-838.
3. Lynn EG, Siow YL, O K: Very low density lipoprotein stimulates the expression of monocyte chemoattractant protein-1 in Mesengialcells. Kidney Int 2000; 57: 1472-1483.
4. Hattori M, Nikolic-Paterson DJ, Miyazaki K, Isbel NM, Lan HY, Atkin RC, Kawaguchi H, HIto K; Mechanism of glomerular macrophage infiltration in lipid- induced renal injury, KidneyIntSuppl 1999; 71: S47-S50.
5. Atchley DH, Lopes-Virella MF, Zheng D, Kenny D, Virella G: Oxidised LDL-antioxidised LDL immune complexes and diabetic nephropathy. Diabetologia 2002; 45: 1562-1571.
6. Han J, Hajjar DP, Zhou X, Gotto AM Jr, Nicholson AC: Regulation of peroxisome proliferator-activated receptor-γ-mediated gene expression: A new mechanism of action for high-density lipoprotein. *J BiolChem* 2002; 277: 23582- 23586.
7. Unnikrishnan AG. Menon UV. Thyroid disorders in india: An epidemiological perspective. *Indian J EndocrMetab* 2011; 15: 78-81.
8. Laurence MD, Carole S. The Thyroid: Pathophysiology and Thyroid Function Testing. In: Carl Burtis, Edward RA, David EB, editors. Tietz textbook of clinical chemistry and molecular diagnostics, 4th ed. New Delhi: Elsevier; 2008, p.2065-2072.
9. ERBA Thyrokit TSH [package insert]. ERBA Diagnostics Mannheim GmbH 2013.
10. ERBA Thyrokit T4 [package insert]. ERBA Diagnostics Mannheim GmbH 2013.
11. ERBA Thyrokit T3 [package insert]. ERBA Diagnostics Mannheim GmbH 2013.
12. Triglyceride set [Kit insert]. Thane (India): Accurex Biomedical, 2013.
13. HDL-cholesterol reagent set [Kit insert]. Boisar (India): Biolab, 2013.
14. Cordon T *et.al*. Am j Med.1977; 62:707.
15. Buccolo G, David M.Clin.Chem.1973; 19:476.
16. Friedewald WT, Levy RI, Fredrickson DS. Estimation of theconcentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. ClinChem 1972; 18: 499-502.
17. da Luz PL, Favarato D, Faria-NetoJr JR, Lemos P; Chagas ACP. High ratio of triglycerides to HDL-cholesterol ratio predicts extensive coronary disease. Clinics. 2008; 63:427-32.
18. Gaziano JM, Hennekens CH, O'Donnell CJ, Breslow JL, Buring JE. Fasting triglycerides, high density lipoprotein, and risk of myocardial infarction, Circulation.1997; 96: 2520-5.
19. Purohit P. Estimation of serum insulin, Homeostasis model assessment –insulin resistance and C-peptide can help identify possible cardiovascular disease risk in thyroid disorder patients.2012;16(7):97-103.

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