

Study of influence of thyroid dysfunction on lipid profile

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Abstract

Introduction: Thyroid function regulates a wide array of metabolic parameters. Thyroid function significantly affects lipoprotein metabolism as well as some cardiovascular disease (CVD) risk factors, thus influencing overall CDV risk. **Aims and objectives:** To study changes in lipoprotein levels in hypothyroidism and hyperthyroidism patients and compare it with matched healthy controls in population. **Results:** In hypothyroidism patients there was decrease in synthesis of cholesterol, serum total and LDL cholesterol levels are increased. In patients with overt hypothyroidism, we found highly significant increase in TC, LDL and HDL values and no significant change in TG and VLDL when compared with controls. Whereas in patients with subclinical hypothyroidism, we found significant increase in TC and LDL while no change in TG, HDL and VLDL when compared with controls. **Conclusion:** Thyroid dysfunction has influence of on lipid profile. In hypothyroidism, though there was decrease in synthesis of cholesterol, serum total and LDL cholesterol levels are increased. This was mainly due to decrease in LDL catabolism. And in overt and subclinical hypothyroidism patients, the lipid profile is clearly atherogenic.

Key Words: lipid, thyroid dysfunction.

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INTRODUCTION

Thyroid dysfunction is very well prevalent in India. Thyroid disease burden in India is approximately 42 millions.¹ The Overall prevalence of 5.4% hypothyroidism, 1.9% hyperthyroidism and 7.4% of autoimmune thyroiditis. The thyroid diseases are more common in females as compared to males. Thyroid function regulates a wide array of metabolic parameters. Thyroid function significantly affects lipoprotein metabolism as well as some cardiovascular disease (CVD) risk factors, thus influencing overall CDV risk^{2,3,4}.

Indeed, even within the normal range of thyroid-stimulating hormone (TSH) values, a linear increase in total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C) and triglycerides (TGs) and a linear decrease in high-density lipoprotein cholesterol (HDL-C) levels has been observed with increasing TSH⁵. Thyroid hormones are recognized as catabolic hormones and they regulate various processes of metabolism⁶. The relationship between thyroid hormones and lipid metabolism is clearly displayed in patients suffering from thyroid dysfunctions. Overt hypothyroid patients show elevated cholesterol and triglyceride (TG) levels while overt hyperthyroid patients show reduced lipid levels⁷. These observations have been shown to extend into the subclinical hypo/hyperthyroid range, suggesting that apart from thyroid hormones, thyroid-stimulating hormone (TSH) exerts independent effects on lipid metabolism. Recent advancement in molecular biology has enlightened us on the potential mechanisms of thyroid hormones and TSH in regulating lipid metabolism. Thyroid hormones have been shown to induce the expressions of 3-hydroxy-3-methyl-glutaryl-CoA reductase (HMG-CoA) reductase (responsible for cholesterol synthesis)⁸, low density lipoprotein receptor

(LDLR) via sterol regulatory element-binding protein-2 (SREBP-2) (responsible the uptake of cholesterol)⁹, lipoprotein lipase (responsible for catabolizing TG-rich lipoprotein)¹⁰, cholesteryl ester transfer protein (responsible for high density lipoprotein (HDL) metabolism)¹¹ and apolipoprotein AV (which reduces the production of hepatic very low density lipoprotein (VLDL)-TG)¹². Thyroid-stimulating hormone has also been shown to induce adipogenesis, lipolysis and increase the activity of HMG-CoA.¹³

AIMS AND OBJECTIVES

To study changes in lipoprotein levels in hypothyroidism and hyperthyroidism patients and compare it with matched healthy controls in population.

MATERIAL AND METHOD

Study design: The present study was conducted in Government Medical College and Hospital, Aurangabad from October 2005 to October 2007. The subjects were those who reported to outpatient department of hospital for complaints related to thyroid dysfunction. The history was taken and complete clinical examination was done. Their blood sample was taken into plain and fluoride bulb after 12 hours fasting. The diagnosis of those patients was confirmed by thyroid function tests.

The patients were categorized into three groups as follows,

1. Hyperthyroidism: Raised T3 and T4 hormones than normal and decreased TSH with clinical features.
2. Overt hypothyroidism: TSH > 12 IU/L along with clinical features of hypothyroidism with decreased T3 and T4 levels.
3. Subclinical hypothyroidism: TSH > 4.5 IU/L with minimal clinical features or no features.

Exclusion criteria

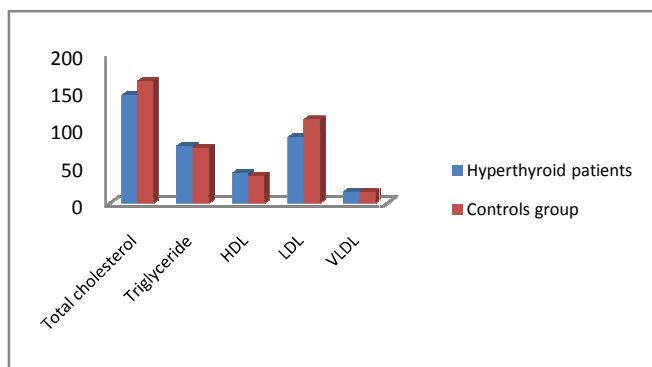
- smoking
- clinical evidence of hepatic or renal disease
- medications known to influence lipid metabolism
- Patients receiving post menopausal replacement therapy.

Age, sex and body mass index matched subjects including males and females were taken as controls. The same exclusion criteria were applied to control subjects as well. Thyroid function test was also conducted in control group and normal levels were confirmed. Simultaneously lipid profile (total cholesterol, triglycerides, HDL, LDL, VLDL) was also done in all the study population. VLDL and LDL were calculated using Friedwald formula. Thus total 25 patients of overt hypothyroidism, subclinical hypothyroidism, hyperthyroidism and control group each were selected.

RESULTS

Table 1: Comparison of lipid profile of hyperthyroid patients with controls group

| Parameters (mg/dl) | Cases (n = 25) mean ± S.D. | Controls (n = 25) mean ± S. D. | p value | Significance |
|--------------------|----------------------------|--------------------------------|---------|--------------------|
| Total cholesterol | 144.7 ± 26.48 | 163.72 ± 27.34 | P<0.05 | Significant |
| Triglyceride | 77.08 ± 18.10 | 74.24 ± 13.8 | P=0.536 | Not significant |
| HDL | 40.56 ± 7.69 | 36.8 ± 8.1 | P=0.082 | Not significant |
| LDL | 88.78 ± 17.95 | 112.33 ± 17.9 | P<0.001 | Highly significant |
| VLDL | 15.41 ± 3.62 | 14.85 ± 2.7 | P=0.542 | not significant |

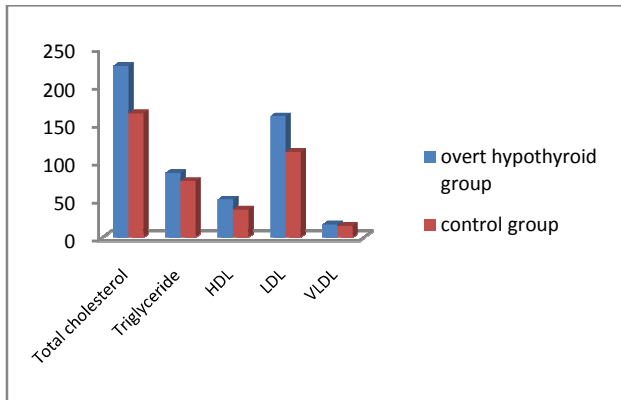


Graph 1: Comparison of lipid profile of hyperthyroid patients with controls group

It was observed that there was decrease in total cholesterol which was significant and also decrease in LDL which was highly significant among the hyperthyroid patients. Whereas the changes in triglycerides, HDL and VLDL were not significant

Table 2: Comparison of lipid profile of overt hypothyroid patients with controls group

| Parameters (mg/dl) | Cases (n = 25) mean± S.D. | Controls (n = 25) mean± S. D. | p value | significance |
|--------------------|---------------------------|-------------------------------|---------|-----------------|
| Total cholesterol | 226.72±54.9 | 163.72±27.34 | P<0.001 | Significant |
| Triglyceride | 85.2 ± 27.5 | 74.24 ± 13.8 | P=0.081 | Not significant |
| HDL | 50.08±13.36 | 36.8 ± 8.1 | P<0.001 | Significant |
| LDL | 159.8 ± 38.2 | 112.33±17.9 | P<0.001 | Significant |
| VLDL | 17.03 ± 5.50 | 14.85 ± 2.7 | P=0.083 | Not significant |

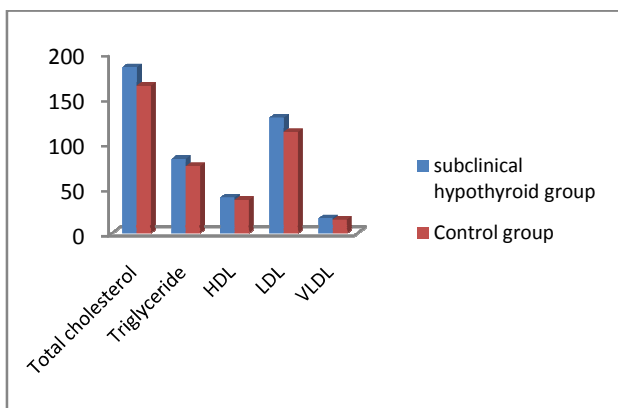


Graph 2: Comparison of lipid profile of overt hypothyroid patients with controls group

When lipid profile of overt hypothyroid patients was compared with control group it was observed that total cholesterol, HDL and LDL were increased in overt hypothyroid group and the difference was highly significant. But the changes in triglycerides and VLDL are statistically not significant.

Table 3: Comparison of lipid profile of subclinical hypothyroid patients with controls group

| Parameters (mg/dl) | Cases (n = 25) mean ± S.D. | Controls (n = 25) mean ± S. D. | p value | Significance |
|--------------------|----------------------------|--------------------------------|---------|-----------------|
| Total cholesterol | 184.28 ± 32.6 | 163.72± 27.3 | P<0.05 | Significant |
| Triglyceride | 82.4 ± 27.06 | 74.24 ± 13.8 | P=0.186 | Not significant |
| HDL | 39.52 ± 12.1 | 36.8 ± 8.1 | P=0.314 | Not significant |
| LDL | 128.28±18.1 | 112.33 ± 17.9 | P<0.05 | Significant |
| VLDL | 16.48 ± 5.41 | 14.85 ± 2.7 | P=0.188 | Not significant |



Graph 3: Comparison of lipid profile of subclinical hypothyroid patients with controls group

In subclinical hypothyroid patients, the table showed increase in total cholesterol and LDL which was statistically significant. The changes in triglycerides, HDL and VLDL were statistically not significant.

DISCUSSION

The present study was conducted at Government Medical College and Hospital, Aurangabad with the objective to study changes the influence of thyroid dysfunction on lipoprotein levels and compare it with matched healthy controls in population. Despite of increased activity of HMG coA reductase, total and LDL cholesterol levels tend to decrease due to increased bile excretion of cholesterol and mainly to increased LDL receptor gene expression resulting in enhanced LDL receptor mediated catabolism of LDL particles. Furthermore, HDL cholesterol levels can decrease in hyperthyroidism due to increased CETP mediated transfer of cholesteryl esters from HDL to VLDL and increased hepatic lipase mediated catabolism of HDL Triglyceride levels remain unchanged. Our study also supports above views. Our study finds significantly decreased levels of total cholesterol and LDL ($p<0.05$, $p<0.001$ respectively) in patients with hyperthyroidism compared with euthyroid patients (control group). Furthermore, our study supports the view proposed by Muls *et al*¹⁴. They studied 33 hyperthyroid patients and compared their lipid profile parameters with normal control subjects. They found statistically significant decreased levels of total cholesterol and LDL. Raziel A¹⁵ studied 11 hyperthyroid patients and compared with age and sex matched controls. They found decreased total cholesterol and LDL values while triglyceride, HDL and VLDL values were unchanged. Our results were similar to their findings. We did not find any change in triglyceride and VLDL in hyperthyroid patients ($p=0.536$, $p=0.542$ respectively). We also did not find any significant change in HDL in hyperthyroid patients ($p< 0.082$). In hyperthyroidism, there is enhanced endogenous de novo synthesis of cholesterol. Even then, these patients exhibit decreased total cholesterol and LDL cholesterol levels in serum because of concomitant increase in LDL catabolism, increase in cholesterol excretion by bile acid and reduced enterohepatic bile acid circulation. The concentration and turnover of free fatty acids are increased in hyperthyroidism, resulting from a thyroid hormone induced increase in lipolysis and increase in oxidation of fatty acids to carbon dioxide as well as to ketone bodies. Hypothyroid patients usually exhibit elevated levels of HDL cholesterol mainly due to increased concentration of HDL2 particles. Decreased activity of CETP results in reduced transfer of cholesteryl esters from HDL to VLDL, thus increasing HDL-C levels. Furthermore, decreased activity of HL leads to decreased catabolism of HDL 2 particles. Our study also supports the above explanation. We found increased levels of total and LDL cholesterol in both overt ($p< 0.001$) as well as subclinically hypothyroid ($p<0.05$) patients while HDL

cholesterol was increased ($p < 0.001$) significantly in only overt hypothyroid patients. It was not significantly changed ($p = 0.314$) in subclinically hypothyroid patients. Erem *et al*¹⁶ studied alterations in lipid profile in thyroid dysfunction. They stated that thyroid hormone regulates lipid metabolism through various mechanisms. The key role was played by LDL receptor pathway. In the present study there was significantly increased LDL and total cholesterol values in overt hypothyroid patients. Razieli A *et al*¹⁵ studied lipid profile in hypothyroid patients and compared with age and sex matched individuals. They found that there is increase in net values of TC, LDL and HDL. We also had similar findings like above publications. Jefery Abrams¹⁷ *et al* studied ten non obese and sixteen obese patients with hypothyroidism. They did not find any change in levels of triglycerides in these patients, as in the case of our study. F. Monzani *et al*¹⁸ found that 45 sub clinically hypothyroid patients had significantly elevated total and LDL cholesterol levels when compared with controls. We have similar findings in our study. Triglycerides and VLDL are not significantly altered when compared with normal control subjects from both groups i.e. overt and sub clinically hypothyroid patients. Thus our study supports most of the publications.

CONCLUSION

Thus in the end we can conclude that thyroid dysfunction has influence of on lipid profile. In hypothyroidism, though there was decrease in synthesis of cholesterol, serum total and LDL cholesterol levels are increased. This was mainly due to decrease in LDL catabolism. And in overt and subclinical hypothyroidism patients, the lipid profile is clearly atherogenic.

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