SPECTRUM OF LIPID ABNORMALITY AMONG THYROID DISORDER PATIENTS IN UCMS-TH, SOUTH WESTERN REGION

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ABSTRACT

INTRODUCTION:

Hypothyroidism is the most common cause of secondary dyslipidemia. Thus, thyroid function test should be carried out before starting any hypolipidemic drugs. Even among thyroid disorder, hypothyroidism is more associated with cardiovascular and associated problems and if not detected earlier, it leads to severe clinical consequences. Our study assesses the frequency and spectrum of dyslipidemia in various types of thyroidal illness in the population residing in south western part of Nepal.

MATERIALS AND METHODS:

This is a cross sectional study carried out in suspected thyroid disorder patients (n=276) and categorized as Euthyroidism (n=55), Subclinical Hypothyroidism (n=89), Primary Hypothyroidism (n=122) and Primary Hyperthyroidism (n=10) patients and to see the association with lipid profiles in the Department of Biochemistry, Universal College of Medical Sciences Teaching Hospital, Bhairahawa Nepal. Serum fT_3 / fT4 and TSH estimations were carried out by competitive ELISA method and Sand-wich double antibody ELISA method respectively using commercially supplied reagents (Human, Germany). The criteria for dyslipidemia was obtained by National Cholesterol Education Expert Panel/ Adult Treatment Protocol III (NCEP/ATPIII).

RESULTS:

Out of 276 cases the dyslipidemia was observed in 183 cases (66.30%).The dyslipidemia was mostly associated with primary hypothyroidism (55.07%) followed by Subclinical Hypothyroidism (38.04%) than Euthyroid (5.79 %) and Primary Hyperthyroidism (3.62 %) respectively. Out of all cases, the spectrum of dyslipidemia was mostly observed for decreased HDL (18.5 %) followed by increased TG (10.1 %). Moreover, it is significantly differ in relation in HDL (p=0.009), TG/HDL (p=0.02) and Non-HDL/HDL (p=0.033) where as non significant as compared to other lipid profile in different groups.

CONCLUSION:

Our study revealed the close association of thyroidal illness with dyslipidemia with increased TG, low HDL, increased TG/HDL and Non-HDL/HDL. The increased TG/HDL and/or Non-HDL/HDL could be better indicator than single lipid abnormality which needs to be ascertained prospectively in large population.

KEY WORDS: Thyroid Disorders; Lipid profile; Thyroid function test; Dyslipidemia

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INTRODUCTION

Thyroid hormones stimulate the secretion of 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase, which is the initial step in cholesterol biosynthesis.[1] Thus, thyroid dysfunction can have an important effect on lipid profile .In most of cases, it was found that as the thyroid hormones decreases , total cholesterol level along with low density lipoprotein tends to increase.[2]Increased levels of TC and LCL-C was seen in subclinical hypokthyroidism.[3]In addition , raised TGs[4] as well as decreased HDL-C levels have been observed in several studies.[5]Hence , screening for thyroid function test should be done while dealing patients with dyslipidemia [6,7,8]But in patients with overt hypothyroidism, activity of HMG-CoA reductase tends to decrease while TC and LDL-C levels are increased.[9,10] This can be explained as increased thyroid hormones leads to decresedcatabolism of LDL and IDL [11,12] Hyperthyroidism canalso be the contributory factor that may cause unexpected improvement of lipid profile in hyperlipidemic patients [13]Since, hyperthyroidism whether overt or subclinical , there is decrease in LDLand HDL cholesterol resulting enhanced oxidation of LDL that depends on level of FT4.[14]Decrease in HDL-C levels is associated with increased CETP-mediated transfer of cholesteryl esters from HDL to VLDL and increased HL-mediated catabolism of HDL_2. [15,16]

Thyroid hormones have been positively correlated with endothelial[17] and cardiac function like atherosclerosis.[18] Defects in lipid metabolism leads to the development of atherosclerotic coronary artery (CAD).[19,20] CVD is not only related with the levels of LDL-C, but even depends on qualitative composition of LDL-C.[21] Hence, alterations in thyroid function not only alter the serum concentration level but also result in changes in the composition and transport of lipoproteins.

Regarding HDL metabolism, thyroid hormones increase cholesteryl ester transport protein (CETP) activity.[22] T_3 upregulates LDL receptors by controlling the LDL receptors gene activation.[23] Among different thyroid disorder, hypothyroidism is prevalent as one of the common causes for secondary dyslipidemia.[24] Therefore, before commencing any therapy for lipid disorder, the evaluation of thyroid function is needed.

Biochemical screening for thyroid dysfunction is critical in all dyslipidemic patients as well as in all patients with unexpected improvement or worsening of their lipid profile. Hence our study can revealed the close correlation of thyroidal illness and various lipid parameters like triglycerides, cholesterol etc.. This is the first kind of study that is undertaking in southwest region of Nepal.

MATERIALS AND METHODS

A cross sectional study was conducted in **Department o**f Biochemistry at Universal College of Medical Sciences (UCMS), Bhairahawa, Nepal. Thyroid disorders was classified as euthyroidism, TSH within the normal range, subclinical hypothyroidism, TSH >4.7mIU/L but normal thyroid hormones, primary hypothyroidism, TSH >4.7mIU/L and primary hyperthyroidism, TSH<0.5mIU/L. Only suspected thyroid disorder patients were enrolled in the study. The consent was taken from each subject and the ethical approval for the study was provided by institute review board of UCMS, Bhairahawa. Serum fT_3 / fT4 and TSH estimations were carried out by competitive ELISA method[4] and Sand-wich double antibody ELISA method[5] respectively using commercially supplied reagents (Human, Germany). The criterion for dyslipidemia was obtained by National Cholesterol Education Expert Panel/ Adult Treatment Protocol III (NCEP/ATPIII).

STATISTICAL ANALYSIS

The data were entered in IBM SPSS Windows version 22 and were expressed as mean and SD values. Independent ttest and Oneway Analysis of Variance (ANOVA) were used. Pearson's correlation coefficient was used to find association between different variables. A P value < 0.05 was considered statistically significant.

RESULTS

Out of 276 cases the dyslipidemia was observed in 183 cases (66.30%) and 90 cases (33.70%) were with normal lipid. Out of all cases, dyslipidemia was mostly associated with primary hypothyroidism (52.46 %), subclinical hypothyroidism (38.26%), euthyroid (5.46%) and primary hyperthyroidism (3.82 %) respectively. The single lipid abnormality was highest in increased LDL (49.8%), decreased HDL (27.8%), increased triglyceride (15.3%) and increased Cholesterol (7.1%) respectively.

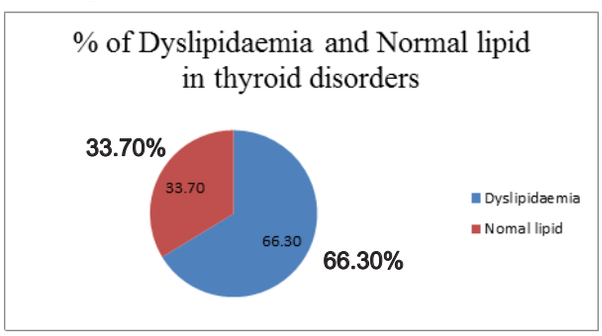

Figure 1: Distribution of Dyslipidaemia in Thyroid disorder Cases (n=276)

Table 1: Distribution of Dyslipidemia in thyroid disorders

Variables (NCEP/ATP III) for dyslipidemia	Euthyroid	Sub Clinical Hypo	Primary Hypo	Primary Hyper	Total (%)
[illegible]	2	3	8	0	13 (7.1)
TG≥150 mg/dl	2	13	11	2	28 (15.3)
LDL≥130 mg/dl	4	31	53	3	91 (49.8)
HDL<40 (M),50 (F) mg/dl	2	23	24	2	51 (27.8)
Total	10 (5.46%)	70 (38.26%)	96 (52.46%)	7 (3.82%)	183 (100%)

The maximum of dyslipidemia was seen observed in isolated decreased HDL (18.5%), combination of increased TG and Decreased HDL (15.2%), increased TG (10.1%) and increased TC (4.7%) respectively.

Table 2: Association between thyroid disorders and spectrum of lipid profile

Lipid statu	Euthyroid	SubClinical Hypo	Primary Hypo	Primary Hyper	Total (%)
Normal lipid level	45	19	26	3	93 (33.7)
Increased TG	2	13	11	2	28 (10.1)
Decreased TC & HDL	0	2	0	1	3 (1.1)
Increased TC & LDL	1	2	5	1	9 (3.3)
Decreased HDL	2	23	24	2	51 (18.5)
Increased TC & TG, Decreased HDL	0	3	4	1	8 (2.9)
Increased TG & Decreased HDL	2	13	27	0	42 (15.2)
Increased TC, TG & LDL, Decreased HDL	1	2	1	0	4 (1.4)
Increased TC	2	3	8	0	13 (4.7)
Increased TC & Decreased HDL	0	3	5	0	8 (2.9)
Increased TG & Decreased TC	0	1	0	0	1 (0.4)
Increased TC & TG	0	5	6	0	11 (4.0)
Decreased TC	0	0	1	0	1 (0.4)
Increased TC & LDL, Decreased HDL	0	0	4	0	4 (1.4)
Total	55	89	122	10	276

There were significant difference in the thyroid hormones ($p<0.0001$), HDL cholesterol ($p<0.009$), TG/HDL ratio ($p<0.024$) and Non-HDL/HDL ratio ($p<0.033$) respectively.

Table 3: Comparison of thyroid hormones and lipid profile in different thyroid disorder

Variables	Euthyroid (n=55)	Sub Clinical Hypo (n=89)	Primary Hypo (n=122)	Primary Hyper (n=10)	p-value (ANOVA)
fT3	2.52±0.56	1.85±0.43	1.43±0.45	4.55±1.10	0.0001
fT4	1.28±0.25	1.05±0.26	0.80±0.15	2.36±0.49	0.0001
TSH	3.68±1.65	7.85±1.07	26.88±18.81	0.15±0.04	0.0001
TC	171.38±43.31	175.48±52.26	173.35±56.52	160.65±82.74	0.148
TG	144.85±26.01	172.95±114.81	160.92±85.66	146.26±95.84	0.302
HDL	54.53±10.18	47.11±13.10	49.72±16.18	43.11±10.10	0.009
LDL	88.30±73.97	100.82±44.26	93.97±44.93	91.08±50.58	0.187
VLDL	28.96±5.18	34.38±22.86	32.53±17.21	29.24±19.17	0.329
TG/HDL	2.76±0.84	3.92±2.70	3.62±2.22	3.61±2.73	0.024
Non-HDL/HDL	2.15±1.01	2.93±1.38	2.71±1.38	2.67±1.24	0.033

There were signaificant difference in thyroid liarmone ($p<0.0001$) HDL cholesterol ($P<0.0001$), TG/HDL ration ($p<0.024$), Non HDL/HDL ration ($p<0.033$) respectively (Table 3)

Table 4:Correlation analysis of the lipid profile with thyroid hormones

Variables	TC	TG	HDL	LDL	VLDL	TG/HDL	Non-HDL/HDL
fT3	-.35	-.121	0.028	-.008	-.127	-.116	-.071
fT4	-.017	-.027	.009	-.001	-0.22	-.025	-.030
TSH	.051	.048	-.095	.050	.057	.106	.015

There were negative correlation of TC, TG, LDL, VLDL, TG/HDL, Non-HDL/HDL with fT3, fT4 and positive correlation of TC, TG, LDL, VLDL, TG/HDL, Non-HDL/HDL with TSH but HDL has negative correlation with HDL. The variables observed to be not statistically significant.

DISCUSSION

Thyroid hormones play a major role in maintaining effective lipid metabolism thus any alteration in these hormone levels lead to drastic change in lipid profile.[2]Out of 273 patients enrolled, dyslipidemia was mostly associated with primary hypothyroidism (52.46 %), subclinical hypothyroidism (38.26%), euthyroid (5.46 %) and primary hyperthyroidism (3.82 %) respectively In our study, hypercholesterolemia along with high triglyceride level was found in primary hypothyroidism followed by subclinical hypothyroidism. Similar findings were also observed in the study of Keyes &Heimberg[25]and Laker & Mayes [26].Likewise LDL level was also found to be increased in hypothyroidism similar to that of fifth Tromso Study.[27] As thyroid secretion decreases, there is decrease in rate of cholesterol secretion in bile thus decreased in excretion of cholesterol in faeces that eventually leads to hypercholesterolemia . Hypercholesterolemia is also associated with elevated level of low density lipoprotein (LDL) and decreased number of low density lipoprotein receptors on the liver cells.[28] Decreased LDL receptors cause diminished receptor mediated catabolism of LDL. IDL is the main cause of the hypercholesterolemia observed in hypothyroidism.[31]According to Nikkilia & Kekki[29], decreased in activity of lipoprotein lipase (LPL) leads to increase in triglyceride level in hypothyroidism which results in decreased clearance of triglyceride-rich lipoproteins.In other hand, there is elevated levels ofhigh density lipoprotein cholesterol (HDL-C) in hypothyroid patients due to increased concentration of HDL2 particles.[30]In our study, decresed HDL

(47.11±13.10) was found to be associated with hypothyroid cases rather than euthyroid ones suggesting a defect in HDL metabolism. Although the observation was confronting one but some of the studies also reproduce the similar results.[12,31] There were significant difference in the thyroid hormones ($p<0.0001$), HDL cholesterol ($p<0.009$), TG/HDL ratio ($p<0.024$) and Non-HDL/HDL ratio ($p<0.033$) respectively. Our study showed that mean HDL level was significantly higher in hypothyroidism but there was no statistically significant difference in the mean LDL, VLDL, cholesterol and triglyceride levels. LDl cholesterol was higher in hypothyroid patients as compared to others .This suggest that hypothyroid patients are at high risk in developing cardiovascular diseases.

Regarding TG/HDL and Non HDL/HDL ratio, the highest average ratio was seen in subclinical hypothyroid patient ($p = 0.024$, $p = 0.033$)since TG and Non HDL cholesterol were found to be markedly increased in such cases. Some studies have also shown that SH dyslipidemia may also be accompanied by increased TGs [12,32] and decreased HDL-C levels.[33]

Different parameters of lipid spectrum was found to be negatively correlated with thyroid hormones (fT3 and fT4).meanwhile positive correlation was seen with that of TSH level. Like some other studies[34], HDL cholesterol was found to be negatively correlated with TSH but the variables observed to be not statistically significant.

CONCLUSION

Our study revealed the close association of thyroidal illness with dyslipidemia with increased TG, low HDL, increased TG/HDL and Non-HDL/HDL. The increased TG/HDL and/or Non-HDL/HDL could be better indicator than single lipid abnormality. Hence, biochemical screening for thyroid dysfunction is critical in all dyslipidemic patients and proper treatment in designated time will prevent the patients from future consequences of developing cardiovascular disease (CVD) like artherosclerosis.

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