



PREVALENCE OF DYSLIPIDEMIA IN PATIENTS OF SUB CLINICAL HYPOTHYROIDISM AND THE EFFECTS OF THYROXINE REPLACEMENT THERAPY ON LIPID PROFILE IN NORTH INDIAN POPULATION

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ABSTRACT

Subclinical hypothyroidism is a very common entity in Indian middle aged population with a prevalence of around 6-15%, defined as increase in thyroid stimulating hormone (TSH) level without obvious rise in free triiodothyronine (FT3) and free thyroxine (FT4) level. However most of the patients have an annual conversion of 5% into overt hypothyroidism. Replacement of thyroxine in these patients is always a controversial issue, deranged lipid profile is an important indication of thyroxine replacement in these patients. In present study which is a case control study, we have observed improvement in lipid profile after thyroxine replacement in patients of subclinical hypothyroidism with deranged lipid profile. In our study there is a significant improvement in total cholesterol, triglyceride, and LDL level without significant improvement in HDL level after thyroxine replacement.

KEYWORDS

subclinical hypothyroidism, thyroxine, lipid profile

INTRODUCTION:

Subclinical hypothyroidism is more common than overt hypothyroidism. Elevated thyroid peroxidase antibodies is found in 73% of subclinical hypothyroidism (SCH) patients. As the value of thyroid peroxidase antibodies goes higher, more rapid thyroid failure is there and since subclinical hypothyroidism patients with positive thyroid peroxidase antibodies have around 5% per year conversion rate into overt hypothyroidism, it is important to screen and diagnose these patients at risk, and hence, thyroid peroxidase antibodies measurement is recommended as an integral part of the investigations done for subclinical hypothyroidism.^{1,2}

Thyroid hormone replacement may prevent progression of subclinical hypothyroidism to overt hypothyroidism, may slow the coronary heart disease progression due to its beneficial effects on lipid and so early diagnosis and early thyroxine treatment are recommended for such patients.³

Treatment of subclinical hypothyroidism is still controversial. If untreated, patients might develop cardiac dysfunction, dyslipidemias, and symptoms of hypothyroidism or progression to overt hypothyroidism and neuropsychiatric symptoms.⁴

MATERIALS & METHODS:

Present study is conducted in P.G. Department of Medicine in S.N. Medical College, Agra. 100 diagnosed subclinical hypothyroid patients (Anti TPO antibody positive) and 100 control patients are included in this study. Patients taking antithyroid medication, hypolipidemic drugs, post thyroid surgery, end stage renal disease, congestive heart failure, diabetes mellitus, myocardial infarction are excluded from this study.

Anti TPO antibody and TSH level was measured by chemiluminescent immunometric assay while lipid profile measurement in these patients is measured by cholesterol esterase method and lipase method.

OBSERVATION AND RESULTS:

In present study 100 patients are included as case and 100 patients are included as control group. In the case group 81% patients were female while 19% patients were male. Similarly in the control group female predominance is again there hence case and control groups were matched for sex distribution.

If we compare thyroid profile of subjects there is statically significant difference found between case and control group for subclinical hypothyroidism (Anti TPO antibody positive) as shown in **Table 1** and **Bar diagram 1** and **2**.

Table – 1 : Thyroid Profile of Subjects.

Parameter	Control		Case		t-value	p-value
	Mean	SD	Mean	SD		
TSH(Miu/L)	3.13	1.05	7.40	1.29	25.58	<0.001
FREET4(ng/dl)	1.89	0.54	1.90	0.47	0.14	0.890
freeT3(Pg/ml)	3.16	0.68	3.37	0.65	2.18	0.030
ANTI TPO(IU/ml)	14.98	8.79	152.25	136.33	10.05	<0.001

The mean TSH of control group was 3.13±1.05 units while in case group it was 7.40±1.29 units. The significant difference was found in mean TSH level between case and control group (p<0.001).

The mean free T4 of control group was 1.89±0.54 units while in case group it was 1.90±0.47 units. No significant difference was found in mean free T4 level between case and control group (p=0.890).

The mean free T3 of control group was 3.16±0.68 units while in case group it was 3.37±0.65 units. The significant difference was found in mean free T3 level between case and control group (p=0.030).

The mean ANTI TPO of control group was 14.98±8.79 units while in case group it was 152.25±136.33 units. The significant difference was found in mean ANTI TPO level between case and control group (p<0.001).



Bar diagram 1: Thyroid profile of subjects.

Bar diagram 2: Anti TPO antibody titre of subjects.

If we compare the lipid profile before thyroxine replacement in subclinical hypothyroidism (Anti TPO antibody positive) there is statically significant difference was found between case and control group as shown in **table 2** and **bar diagram 3**.

Table 2: Lipid Profile of Subjects before the Thyroxine Replacement.

Parameter	Control		Case		t-value	p-value
	Mean	SD	Mean	SD		
S. total CHOLESTROL (mg/dl)	165.12	22.15	247.62	60.62	12.77	<0.001
S. TRIGLYCERIDE (mg/dl)	118.09	20.76	282.66	100.50	16.03	<0.001
S.HDL(mg/dl)	59.23	12.21	48.86	8.99	-6.82	<0.001

S.LDL(mg/dl)	98.99	16.78	171.93	30.38	20.99	<0.001
S.VLDL(mg/dl)	25.14	7.27	35.23	5.11	11.32	<0.001

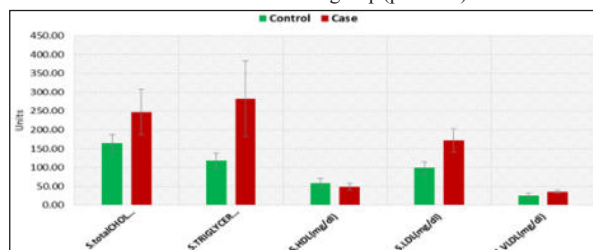
The mean Total Cholesterol of control group was 165.12±22.15 units while in case group it was 247.62±60.62 units. The significant difference was found in mean Total Cholesterol level between case and control group (p<0.001).

The mean TG of control group was 118.09±20.76 units while in case group it was 282.66±100.50 units. The significant difference was found in mean TG level between case and control group (p<0.001).

The mean HDL of control group was 59.23±12.21 units while in case group it was 48.86±8.99 units. The significant difference was found in mean HDL between case and control group (p<0.001).

The mean LDL of control group was 98.99±16.78 units while in case group it was 171.93±30.38 units. The significant difference was found in mean LDL level between case and control group (p<0.001).

The mean VLDL of control group was 25.14±7.27 units while in case group it was 35.23±5.11 units. A significant difference was found in mean VLDL between case and control group (p<0.001).



Bar diagram 3: Lipid Profile of Subjects before the Thyroxine Replacement.

In present study we again compare the effect of thyroxine replacement on the lipid profile of the patients of subclinical hypothyroidism (Anti TPO positive). There is a significant improvement in lipid profile of patient of subclinical hypothyroidism (Anti TPO antibody positive) after thyroxine replacement as shown in **table 3** and **bar diagram 4** and **bar diagram 5**.

Table 3: Comparison of Baseline and Final Lipid Profile between the Thyroxine Replaced and Not Replaced Cases.

	Lipid	Thyroxine Replaced		Thyroxine Not Replaced		t-value	p-value
		Mean	SD	Mean	SD		
Baseline	S.totalCHOLESTROL(mg/dl)	261.65	54.25	184.44	46.60	5.59	<0.001
	S.TRIGLYCERIDE(mg/dl)	300.47	96.17	202.50	79.93	4.02	<0.001
	S.HDL(mg/dl)	48.72	9.18	49.50	8.25	-0.33	0.740
	S.LDL(mg/dl)	177.88	26.72	145.17	32.14	4.52	<0.001
	S.VLDL(mg/dl)	34.80	5.02	37.17	5.20	-1.80	0.076
Final	S.totalCHOLESTROL(mg/dl)	192.17	20.20	183.06	31.01	1.56	0.123
	S.TRIGLYCERIDE(mg/dl)	183.98	38.16	169.78	43.23	1.39	0.167
	S.HDL(mg/dl)	48.69	8.35	49.72	8.19	-0.48	0.635
	S.LDL(mg/dl)	117.63	17.62	109.11	17.71	1.85	0.067
	S.VLDL(mg/dl)	32.98	4.86	36.00	4.78	-2.39	0.019
Change (BL to Final)	S.totalCHOLESTROL(mg/dl)	69.48	43.68	1.39	17.65	6.48	<0.001
	significance	t=14.49, p<0.001		t=1.39, p=0.743			
	S.TRIGLYCERIDE(mg/dl)	116.49	75.24	32.72	50.91	4.49	<0.001
	significance	t=13.91, p<0.001		t=2.73, p=0.014			
	S.HDL(mg/dl)	-0.02	2.47	0.22	1.63	-0.40	0.687
	significance	t=0.14, p=0.893		t=0.58, p=0.570			
	S.LDL(mg/dl)	60.25	23.58	36.06	24.82	3.90	<0.001
	significance	t=23.30, p<0.001		t=6.16, p<0.001			

S.VLDL(mg/dl)	1.83	4.71	1.17	5.23	0.53	0.599
significance	t=3.49, p=0.001		t=0.95, p=0.357			

At final observations (after intervention) the mean Total Cholesterol of thyroxine replaced cases was 192.17±20.20 units while in not replaced cases it was 183.06±31.01 units. No significant difference was found in mean Total cholesterol level between thyroxine replaced and not replaced cases (p=0.123).

The mean TG of thyroxine replaced cases was 183.98±38.16 units while in not replaced cases it was 169.78±43.23 units. No significant difference was found in mean TG between thyroxine replaced and not replaced cases (p=0.167).

The mean HDL of thyroxine replaced cases was 48.69±8.35 units while in not replaced cases it was 49.72±8.19 units. No significant difference was found in mean HDL between thyroxine replaced and not replaced cases (p=0.635).

The mean LDL of thyroxine replaced cases was 117.63±17.62 units while in not replaced cases it was 109.11±17.71 units. No significant difference was found in mean LDL between thyroxine replaced and not replaced cases (p=0.067).

The mean VLDL of thyroxine replaced cases was 32.98±4.86 units while in not replaced cases it was 36.00±4.78 units. The significant difference was found in mean VLDL between thyroxine replaced and not replaced cases (p=0.019).

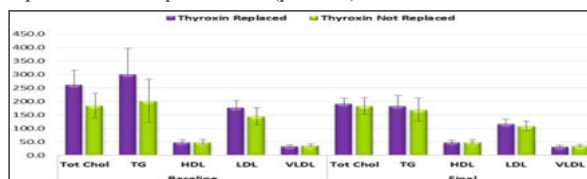
The difference in Lipid profile between initial and final observations shows that the mean change in Total Cholesterol of thyroxine replaced cases was 69.48±43.68 units while in not replaced cases it was 1.39±17.65 units. The significant difference was found in mean change in Total cholesterol level between thyroxine replaced and not replaced cases (p<0.001).

The mean change in TG of thyroxine replaced cases was 116.49±75.24 units while in not replaced cases it was 32.72±50.91 units. The significant difference was found in mean change in TG between thyroxine replaced and not replaced cases (p<0.001).

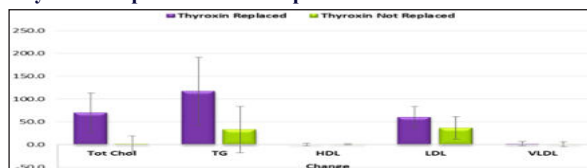
The mean change in HDL of thyroxine replaced cases was -0.02±2.47 units while in not replaced cases it was 0.22±1.63 units. No significant difference was found in mean change in HDL between thyroxine replaced and not replaced cases (p=0.687).

The mean change in LDL of thyroxine replaced cases was 60.25±23.58 units while in not replaced cases it was 36.06±24.82 units. The significant difference was found in mean change in LDL between thyroxine replaced and not replaced cases (p<0.001).

The mean change in VLDL of thyroxine replaced cases was 1.83±4.71 units while in not replaced cases it was 1.17±5.23 units. No significant difference was found in mean change in VLDL between thyroxine replaced and not replaced cases (p=0.599).



Bar Diagram 4: Comparison of Baseline Lipid Profile between the Thyroxine Replaced and Not Replaced Cases.



Bar Diagram 5: Comparison of Final Lipid Profile between the Thyroxine Replaced and Not Replaced Cases.

DISCUSSION:

Subclinical hypothyroidism is known to be associated with disorder in lipids, characterized by normal or high total cholesterol, raised LDL, serum TG, and dense LDL-C (sd LDL-C) level and lower level of

HDL.^{5,6} Subclinical hypothyroidism is also related with endothelial dysfunction, aortic atherosclerosis and myocardial infarction. Subclinical hypothyroidism patients with positive thyroid peroxidase antibodies have around 5% per year conversion rate into overt hypothyroidism. Overt hypothyroidism is associated with increased risk of cardiovascular disease, which is attributed to increased TC and LDL-C.

Elevation of plasma LDL-C is due to impaired clearance of LDL, probably reflecting decrease LDL receptor expression.⁷ Thyroid hormone has a great impact on lipid metabolism, as it is needed for catabolism and synthesis of lipids and its deficiency may create alteration in lipid metabolism probably as a result of its predominant effect on degradation of lipid.

The lipid lowering effect of thyroxine in patients with SH is not yet established. Multiple interventional studies have evaluated the effects of L-thyroxine treatment on lipid profiles in patients with subclinical hypothyroidism, with mixed results.

In our study Anti TPO antibody of control group was 14.98+ 8.79 units while in case group it was 152.25+136.33 units. The significant difference was found in mean Anti TPO antibody level between case and control group ($p<0.001$). This was seen in other studies also such as **Vikas Kumar Srivastava et al(2017)**⁸, **Sanjay K Bhandopadhyay et al(2006)**⁹, **John P Walsh et al(2005)**¹⁰ where Anti TPO antibody level was seen abnormal in 56% of case group. In these studies most of the cases with abnormal TPO levels were found in females as shown in our study.

Among cases most of variables such as serum cholesterol, serum triglyceride, serum LDL were found to be significantly abnormal while serum HDL is not so abnormal. This was similar to other studies such as **Vikas Kumar Srivastava et al(2017)**⁸, **Pala NA et al(2017)**¹¹, **Maida SeferovicSaric et al(2017)**¹² in which significantly higher levels of total cholesterol, serum triglycerides, serum LDL, were seen but level of serum HDL was insignificantly lowered in most of the patients.

In our study the mean change in TG of thyroxine replaced cases was 116.49±75.24 units while in not replaced cases it was 32.72±50.91 units. The significant difference was found in mean change in TG between thyroxine replaced and not replaced cases ($p<0.001$). The mean change in HDL of thyroxine replaced cases was -0.02±2.47 units while in not replaced cases it was 0.22±1.63 units. No significant difference was found in mean change in HDL between thyroxine replaced and not replaced cases ($p=0.687$). The mean change in LDL of thyroxine replaced cases was 60.25±23.58 units while in not replaced cases it was 36.06±24.82 units. The significant difference was found in mean change in LDL between thyroxine replaced and not replaced cases ($p<0.001$).

This results are similar to **Ajay Asranna et al (2012)**¹³ whose study shows that TSH dependent increase in cholesterol, LDL, VLDL, Triglyceride level and by thyroxine replacement euthyroid state can be achieved which has favourable effect on lipid profile. Similar observation was made by **Christian Meier(2002)**¹⁴ whose study evaluated the effect of L-thyroxine treatment on serum lipids and clinical symptoms in patients with subclinical hypothyroidism. In the L-thyroxine replaced group, total cholesterol and low density lipoprotein cholesterol were significantly reduced by 3.8% and 8.2% respectively. These changes are consistent with our study thus we can conclude that thyroxine replacement appears to be a valid indication in patients of subclinical hypothyroidism with deranged lipid profile.

CONCLUSION:

With increasing prevalence of coronary artery disease in women more and more interest is emerging to know the contributing factor for CAD in women which can be easily reversible. In patients of sub clinical hypothyroidism which is very common in female deranged lipid profile is an important contributing factor which can be easily reversed by thyroxine replacement as shown in our study. However limitations of our study is that it is a single centre based observational case control study having a small sample size and results cannot be applied into general population. Further research with large sample size and cross regional study to validate our results are needed.

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