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IMPACT OF LEVOTHYROXINE SUPPLEMENT ON TRIGLYCERIDES AND VERY LOW-DENSITY LIPOPROTEINS IN HYPOTHYROID PATIENTS

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ABSTRACT: Our aim is to observe the impact of Levothyroxine supplement on Triglycerides and Very- low-density lipoproteins in Hypothyroid patients. This study is to observe the incidence of Dyslipidemia condition (elevated TG's, VLDL levels) and the impact of levothyroxine supplement on TG's and VLDL in hypothyroidism patients. Our current study is an observational study, which involves observation of hypothyroid patients and their TSH levels, TG's, VLDL levels. The results showed that, out of 150 patients, 65 people came under group I, and 85 people were under group II. In Group-I, patients with elevated TG's and VLDL's were found to be 10(15. 38%), 6(9.23%) respectively. Similarly, in Group-II, patients with elevated TG's and VLDLs were found to be 46(54.11%), 38(65.51%), respectively. Finally, we conclude that treatment with levothyroxine in patients with a history of hypothyroidism above 5 years resulted in the maintenance of normal TSH levels, TG's and VLDL levels when compared with those patients who had a history of hypothyroidism below 5 years with elevated TSH, TG's and VLDL levels.

INTRODUCTION: Thyroid diseases are among the commonest endocrine disorders worldwide. India too is no exception. According to a projection from various studies on thyroid disease, it has been estimated that about 42 million people in India suffer from thyroid diseases. Early diagnosis and treatment remain the cornerstone of management [1].

Lipids: Lipids are the substances that may be called organic substances relatively insoluble in water, soluble in organic substances, and they are related to fatty acids and utilized by the living cells [2].

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Lipid Metabolism: Increased thyroid hormone levels stimulate fat mobilization, resulting in increased concentrations of fatty acids in plasma. They also enhance the oxidation of fatty acids in many tissues. Finally, plasma concentrations of cholesterol and triglycerides are inversely correlated with thyroid hormone levels - one diagnostic indication of hypothyroidism is increased blood cholesterol concentration [3].

Effect of Thyroid Hormone on Lipid Metabolism: Thyroid hormones stimulate lipolysis from fat stores in white adipose tissue and from dietary fat sources to generate circulating free fatty acids (FFAs), which are the major source of lipids for the liver. FFAs enter hepatocytes *via* protein transporters such as fatty acid transporter proteins (FATPs), liver fatty acid-binding proteins (L-FABPs) and fatty acid translocase [4].

Regulation of lipid metabolism on the liver by the thyroid is primarily dependent on specific actions on thyroid receptors. Thyroid hormone influences lipid metabolism majorly through the following mechanisms. It includes: a) Inhibiting HMG-CoA reductase, b) Enhancing elimination of cholesterol in bile. c) Activation of corepressor d) Action at LDL receptor[2].

Link between Dyslipidemia and Hypothyroidism: The hypothyroid function is accompanied by reduced activity of HMG-CoA reductase, TC, and LDL-C levels are increased in patients with hypothyroidism. This is due to the decreased LDL-receptors activity, resulting in decreased catabolism of LDL, IDL, and decreased clearance of TG-rich lipoproteins. Elevated TG levels associated with increased levels of VLDL and occasionally fasting chylomicronemia can also be observed in hypothyroid patients.

Hypothyroid patients may also exhibit elevated levels of HDL-C mainly due to increased concentration of HDL_2 particles. A decrease in HDL_2 catabolism may be due to a reduction of HL activity. Moreover, decreased activity of the CETP results in a reduced transfer of cholesteryl esters from HDL to VLDL, thus increasing HDL-C levels. Hypothyroid patients have increased lipoprotein (a) levels, which are associated with increased CVD risk. Beyond the levels of LDL-C, the qualitative composition of LDL-C plays an important role in CVD development[5].

Aim: To observe the impact of Levothyroxine supplement on Triglycerides and Very low-density lipoproteins in Hypothyroid patients.

Objectives:

- To observe the incidence of Dyslipidemia condition (elevated TG's, VLDL levels) in hypothyroidism patients with normal and elevated levels of TSH.
- To observe the TG's and VLDL levels in hypothyroidism patients with comorbid conditions *i.e.,* Hypertension and Diabetes.
- To observe the impact of levothyroxine on TG's and VLDL in hypothyroidism patients with a history of onset of disorder above and below 5 years.

MATERIALS AND METHODS:

Study Design: Our current study is an observational study, which involves observation of hypothyroid patients and their TSH levels, TG's, VLDL levels visiting the surgical outpatient department of our hospital.

Study Duration: The study was conducted in the following five months duration *i.e.,* from August-2019 to December-2019.

Study Criteria:

Inclusion Criteria:

- Patients who are willing to participate in the study.
- Patients of either sex.
- Patients with comorbid conditions like hypertension, diabetes mellitus.
- Patients who possess sufficient data were included in our study.

Exclusion Criteria:

- Patients who are not willing to participate in the study.
- Patients who were pregnant and lactating.
- Patients who did not possess sufficient data for our study were excluded.

Study Population Size: Individuals with Hypothyroidism who were visiting the Surgical outpatient department at the Government hospital during our study period were approached to take part in the study. The study population size is 150.

Study Materials: The materials used in the study were

1. VLDL and TG's values.
2. Thyroid-stimulating hormone value.

Study Methods:

1. Data Collection Process:

a. A patient-specific data was collected from patients during the study period.

b. The obtained patient-specific data was entered into data collection forms.

2. Data collection was done between August-2019 to December-2019.

3. Measurement of TSH and lipid levels:

To evaluate thyroid-stimulating hormone levels and lipid levels (TG's, VLDL's), we have taken the blood samples of the patient.

4. We thoroughly checked the patients data to know whether patients had any comorbid conditions like hypertension and diabetes were noted.

5. Data Management: All the data were recorded in Microsoft excel. Statistics were carried out, and the results were reported.

Our article has been approved by IRB (Institutional Review Board)

IRB No: SIRCRRCOPS/IRB/2019-2020/03.

RESULTS: We have collected the data of 150 cases of hypothyroid patients who have visited the government hospital during the study period.

The following are the results obtained from our study.

TABLE 1: DISTRIBUTION OF PATIENTS BASED ON GENDER

S. no.	Gender	No of Patients (N=150)	Percentage (%)
1	Male	7	5
2	Female	143	95

The above data shows that out of 150 patients, 143 were females and 7 were males.

TABLE 2: DISTRIBUTION OF PATIENTS BASED ON AGE

S. no.	Age (In Years)	No. of Patients (N=150)	Percentage (%)
1	11-20	3	2
2	21-30	46	30.66
3	31-40	48	32.0
4	41-50	35	23.33
5	51-60	14	9.33
6	61-70	4	2.66

According to age analysis, number of patients in age group of 11-20, 21-30, 31-40, 41-50, 51-60, and 61-70 are 3 (2%), 46(30.66%), 48(32.0%), 35(23.33%), 14(9.33%) and 4(2.66) respectively. This data reveals that patients aging between 31-40 years were found to be high followed by 21-30 age group.

TABLE 3: DISTRIBUTION BASED ON SYMPTOMS

S. no.	Symptom	No. of Patients (N=150)	Percentage (%)
1	Hair loss	146	97.3
2	Tiredness	149	99.3
3	Headache	116	77.3
4	Insomnia	79	52.6
5	Loss of appetite	73	48.6
6	Menstrual disturbances	42	29.37

We have collected all the symptoms of hypothyroidism which are of major concern in our patients. All the symptoms were arranged in ascending manner in the above data. Out of 150 patients, the symptoms are recorded as tiredness, hair loss, headache, insomnia, loss of appetite, menstrual disturbances of number 149, 146, 116, 79, 73 and 42 respectively.

A Comparison between >5 Years and <5 Years of Age: The data shown below were divided into two groups based on the history of hypothyroidism, intake of levothyroxine supplement of age above (Group-I) and below 5 years (Group-II), and also with dyslipidemia condition. The data were divided into two groups based on the Supriya Shrimant Ohal *et al*., study. Out of 150 patients, 65comes under the category of history of hypothyroidism above 5 years, and 85 comes under the category of history of hypothyroidism below 5 years [6].

A Comparison between Triglycerides and VLDL in Elevated TSH Patients: The incidence of Dyslipidemia condition (*i.e.*, TG's, VLDL levels) in elevated patients considering TSH (Thyroid Stimulating Hormone) as a parameter of categorization between them is observed. The patients were divided into two groups containing 15 members in Group-I (>5 years with elevated TSH) and 51 members in Group-II (<5 years with elevated TSH).

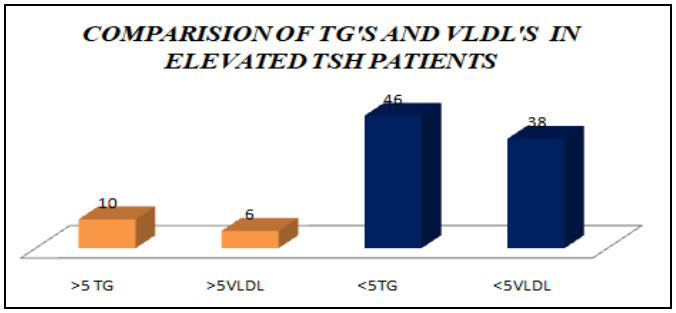

FIG. 1: COMPARISON OF TG's AND VLDL's IN ELEVATED TSH PATIENTS BELONGING TO GROUPS-I AND II

TABLE 4: COMPARISON BETWEEN TG's AND VLDL PARAMETERS

S. no.	Parameter	Group-I (>5years)	Group-II (<5years)
1	Triglycerides	10(15.38%)	46(54.11%)
2	Very low density lipoproteins	6(9.23%)	38(65.51%)

The above data shows that subjects with elevated TG's and VLDL are 10(15.38%), 6(9.23%) and 46(54.11%), 38(65.51%) in groups - I, II respectively.

Statistical Analysis: Statistical analysis in two groups was performed using the Chi-square test in order to assess the relationship between variables.

CHI-SQUARE TEST FOR NORMAL TSH PEOPLE

Group	TG's and VLDL (Elevated)	TG's and VLDL (Normal range)
>5 years	10	36
<5 years	18	10
O	**E**	**$\Sigma(O-E)^2/E$**
10	17.4	3.14
36	28.59	1.92
18	10.59	5.18
10	17.4	3.14
χ^2 =		13.38

Since it is a 2 × 2 contingency table for both cases, rows and columns are the same in number. The degree of freedom is 1. The critical value is 3.84 at 5% level of significance (LOS).

Here the Null Hypothesis is Stated as (H_0): There is no significant relationship between intake of levothyroxine supplement and maintenance of normal TG's and VLDL levels.

Alternate Hypothesis is Stated as (H_1): There is a significant relationship between intake of levo-thyroxine supplement and maintenance of normal TG's and VLDL levels.

Therefore, based upon calculation, calculated value (13.38) > critical value (3.84). So reject H_0 and accept H_1.

CHI-SQUARE TEST FOR ABNORMAL TSH PEOPLE

Group	TG's and VLDL (Elevated)	TG's and VLDL (Normal range)
>5 years	15	0
<5 years	51	10
O	**E**	**$\Sigma(O-E)^2/E$**
15	13.0	0.30
0	1.97	1.96
51	52.9	0.06
10	8.0	0.5
χ^2 =		2.82

Since it is a 2 × 2 contingency table for both cases, rows and columns are the same in number. The degree of freedom is 1. The critical value is 3.84 at 5% level of significance (LOS).

Here the Null Hypothesis is Stated as (H_0): There is no regular intake of levothyroxine supplement and improper maintenance of normal TG's and VLDL levels.

Alternate Hypothesis is Stated as (H_1): There is regular intake of levothyroxine supplement and proper maintenance of normal TG's and VLDL levels.

Thus, based upon calculation, calculated value (2.82) < critical value (3.84). So accept H_0 and reject H_1.

Hence, from the statistical data, we observed that the regular intake of levothyroxine supplement resulted in maintenance of normal levels of triglycerides and very-low-density lipoproteins in Group-I (Normal TSH) when compared to those people of Group-II (Abnormal TSH).

DISCUSSION: In our present study, a total of 150 hypothyroid patients were observed. Among those 150 patients, 7 (5%) were males and 143(95%) were females. In the Saxena *et al.*, study, the predominance of females was noted in cases of hypothyroidism with M to F ratio is 1:6.5. Other studies also reported that hypothyroidism was more prevalent among females than males [7, 8, 9].

In our study, the maximum number of patients of age group 31-40 was found to be 48 (32.0%) followed by 21-30 age group as 46 (30.06%).

In hypothyroid patients, we have collected all the symptoms which are of major concern. Among those 150 patients, the symptoms were observed as tiredness in 149(99.3%), hair loss in 146(99.3%), headache in 116(77.3%), insomnia in 79(52.6%), loss of appetite in 73(48.6%), menstrual disturbances in 42(28%) people.

Based on the evidence from Supriya Shrimant Ohal *et al.*, study[6], our data were divided into two groups based on patients taking levothyroxine supplements from 5 years above and those who are taking from below 5 years. Out of 150 patients, 65 people came under Group I and 85 people were under Group II.

Our results shows that in Group-I, subjects with elevated TG's and VLDL's were found to be 10(15.38%), 6(9.23%), respectively. Similarly, in Group-II, subjects with elevated TG's and VLDLs were found to be 46(54.11%), 38(65.51%), respectively. So, we conclude that people in Group-I have decreased lipid levels when compared with Group-II. These findings were in accordance with Supriya Shrimant Ohal *et al*., which shows that decreased values of TC, TG, LDL-C, VLDL-C, and increased HDL-C were observed in Group-III as compared to Group-II.

And also our study was in accordance with Saxena A *et al.*, who observed increased TC, TG, LDL-C and decreased HDL-C levels in hypothyroid patients and a significant decrease in TC, TG, LDL-C, VLDL levels and increased HDL-C level after levothyroxine treatment [10], but in our study TC levels remain the same and HDL-C levels were omitted.

Our study also matches with Muli Mersudin *et al.*, which shows that after eight weeks of levo-thyroxine replacement therapy, there was a statistically significant reduction of average values of lipid levels [11].

Tehrani *et al.*, estimated that about 2-20% of people in the world are suffering from hypothyroidism, and its prevalence is influenced by geographic location, sex, diet, and race [12].

From our data, we also observed the comorbid conditions relating to hypothyroidism. Out of 150 patients 30 were found to have comorbid conditions like hypertension and diabetes and 15 each came under Group-I and Group-II respectively. Finally, we conclude that comorbid conditions have no significant impact on dyslipidemia conditions.

CONCLUSION: From our study, we conclude that treatment with levothyroxine in patients with a history of hypothyroidism above 5 years resulted in the maintenance of normal TSH levels, TG's and VLDL levels when compared with those patients who had a history of hypothyroidism below 5 years with elevated TSH, TG's and VLDL levels. Due to irregular intake of levothyroxine supplement resulted in increased levels of triglycerides and very low density lipoproteins in patients with a history of hypothyroidism below 5 years.

Elevated levels of triglycerides and very-low-density lipoproteins are a major risk for cardiovascular complications for hypothyroid patients.

The prevalence and severity of cardio-vascular complications depend upon the prognosis of the disease. To minimize the incidence of cardio-vascular complications, the healthcare system should promote continuous monitoring of hypothyroidism. Comorbid conditions have no significant impact on both groups of patients.

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CONFLICTS OF INTEREST: Nil.

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