Effect of Levothyroxine on Lipid Profile in Hypothyroid Patients Attending in a Tertiary Care Hospital

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Abstract

Background:
Hypothyroidism is a common endocrine disorder in our country and is associated with many biochemical abnormalities.Clinical data suggest that levothyroxine replacement therapy has beneficial effect on lipid profile.

Objective:
The present study intends to find out the effect of levothyroxine replacement therapy on lipid profile in hypothyroid patients.

Methods:
A prospective analytical study was done in Endocrinology Outpatient Department of Dhaka Medical college and Hospital, Dhaka from January 2022 to December 2022. A total of 30 newly diagnosed hypothyroid patients were included according to selection criteria. The patient's demographic, past, present history and relevant data needed for the study were collected by face-to-face interview by using structured questionnaire. Baseline data of serum free thyroxine (FT4), thyroid stimulating hormone (TSH), fasting lipid profile, Blood pressure and clinical features of hypothyroidism were recorded in a data collection form during first visit and after 3 months follow up. All patients were treated with tablet levothyroxine and dose was adjusted 4-6 weekly till patients were biochemically euthyroid.

Results:
30 hypothyroid patients were followed up for 3 months. There was significant improvement in hypothyroid symptoms after thyroxine replacement. The mean age of the patient was 35.40±11.52 years. Mean FT4 level was significantly increased from 8.06±3.78 to 16.40±3.95($p<0.001$). There was significant reduction in mean TSH from 32.55±37.31 to 2.52±2.71($p<0.001$). Mean Total cholesterol, TG, LDL-C level was significantly decreased from 193.27±41.69, 173.33±63.71, 119.58±40.11 to 177.80±38.17, 155.87±58.25, 103.07±26.25 ($p=0.022$, 0.044, 0.042) respectively, but HDL has decreased from 45.04±13.14mg/dl to 43.11±10.78 mg/dl ($p=0.415$) though not significantly.

Conclusion:
Thyroxine replacement therapy improves lipid profiles and enhances quality of life. Levothyroxine directly reduces TC, LDL-C, and TG levels but not HDL-C.

Keywords: Hypothyroidism, Levothyroxine, Thyroid stimulating hormone, Total cholesterol, Triglycerides

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Introduction:

Hypothyroidism, caused by low thyroid hormone levels, slows body functions. It can occur with or without goiter. Diagnosis in adults is confirmed by low free thyroxine and high TSH levels.[1] Of the nearly 30 million people estimated to be suffering from thyroid dysfunction most have hypothyroidism.[2] In the recent National Health and Nutrition Examination survey (NHANES III) survey of 17,353 Americans the prevalence of sub clinical hypothyroidism and overt hypothyroidism was respectively 0.3 and 4.3% and was higher in

Caucasians than in Hispanics and Blacks. Ansari (2014) reported that around 10% of the Bangladeshi people suffer from clinically evident thyroid disorder.[3] Hypothyroidism affects up to 5% of the general population, with an estimated additional 5% going undiagnosed. Over 99% of patients with hypothyroidism suffer from primary hypothyroidism, diagnosed biochemically as serum TSH concentrations below normal. Levothyroxine is the standard medication for managing this common disease, which is caused by the immune system attacking the thyroid gland. Symptoms include menstrual irregularities, weight gain, fatigue, and depression, with potential risks like cardiovascular disease if untreated. Levothyroxine is widely prescribed to treat hypothyroidism, with an initial dose of 1.6µg/kg/day and titration to reach optimal TSH levels. Iodine deficiency is a common worldwide cause, and the synthetic T4 hormone levothyroxine is commonly used for hormone replacement therapy.[4] It has been reported that 95% of newly diagnosed hypothyroid patients have increased level of cholesterol and 5% of hypothyroid patients have hypertriglyceridemia. Hypothyroidism leads to a decreased level of the Low density lipoprotein (LDL) receptor expression on fibroblast and hepatocyte, decreased LDL-C (Low density lipoprotein-cholesterol) uptakes and consequent increase in serum LDL-C level.[4] Two other scientists have also observed higher levels of total cholesterol and LDL-cholesterol in both subclinical and overt hypothyroidism.[5,6] Hypothyroidism significantly affects lipid metabolism, especially in patients with high TSH levels. There is a strong correlation between elevated TSH levels and increased total cholesterol and LDL cholesterol. Treatment with thyroxine often improves lipid profiles. In newly diagnosed hypothyroid patients, HDL cholesterol levels are higher (above 40mg/dl) compared to euthyroid and patients on thyroid replacement therapy.[7] Researcher Nikkilᾶ and Kekki have stated that hypertriglyceridemia in hypothyroidism is due to decreased activity of LPL, which results in decreased clearance of triglyceride rich lipoproteins.[8] Hypothyroidism patients usually exhibit elevated levels of highdensity lipoprotein cholesterol mainly due to increased concentration of HDL2 (High density lipoprotein) particles. Decreased thyroid secretion greatly increases the plasma concentration of triglycerides (TG).

Methods:

This prospective analytical study was conducted in the Department of Pharmacology in Dhaka Medical College from January to December 2022. Baseline characteristics were age, gender and family history of hypothyroidism and clinical variables were clinical features of hypothyroidism. Laboratory result of fasting Blood lipid profile e.g TC (total Cholesterol), LDL, HDL, and TG; serum free thyroxine (FT4) and thyroid stimulating hormone (TSH). 30 adult patients (purposive sampling) aged ≥18 years diagnosed with primary hypothyroidism (both overt and Subclinical hypothyroidism) after matching inclusion criteria, were enrolled from Endocrinology Outpatient Department. Exclusion criteria was patient with serious comorbid diseases (Diabetes Mellitus, Myocardial Infarction, Hypertension etc.), secondary hypothyroidism, history of using drugs such as lipid lowering drugs, glucocorticoids, oral contraceptives or vitamin supplements, female patients with pregnancy and taking oral contraceptive pills. Baseline data of FT4, TSH, Anti-thyroglobulin and Anti-thyroid peroxidase bodies levels, fasting lipid profile, Blood pressure and other symptoms of hypothyroidism were recorded in a data collection form during the first visit. All patients were treated with tablet levothyroxine and dose was adjusted 4-6 weekly till patients were biochemically euthyroid. After 12 weeks of follow up, FT4, TSH, fasting lipid profile, Blood pressure, symptoms of hypothyroidism were recorded in the data collection form. Informed written consent paper and specially designated data collection form were filled. The study was done after the approval of Research Review Committee of Dhaka Medical College and ethical clearance was undertaken by Ethical Review Committee of the same institute. Collected data was analyzed by SPSS 26.0 version. Statistical analysis was done by using appropriate statistical tools like, chi-square test and fisher exact test for categorical variables and paired t-test for mean of two groups. The p value ≤0.05 was considered as statistically significant at 95% CI (confidence interval).

Results:

The study examined how levothyroxine replacement impacts lipid profile in hypothyroid patients. Table-I displayed sociodemographic details, with a mean age of 35.40±11.52 years and

a range of 19.0-62.0. Most patients were in the 20-29 age group (36.7%). Females comprised 96.7% and 20% had a family history of hypothyroidism.

Table-I: Sociodemographic characteristics of the study patients (N=30)

Sociodemographic characteristics	no. (%)
Age group (years)	
<20	1(3.3)
20-29	11(36.7)
30-39	8(26.7)
40-49	5(16.7)
50-59	4(13.3)
60-69	1(3.3)
Sex	
Male	1 (3.3)
Female	29(96.7%)
Family history of hypothyroidism	
Present	6(20)
Absent	24(80)

Table-II showed clinical features of hypothyroidism of the study patients before and 3 months after levothyroxine replacement. Most of the patients presented with vague symptoms like general weakness which was significantly changed from (73.3% to 40.0%, p=0.010), Others symptoms which were significantly changed after treatment like weight gain (56.7% to 16.7%, p=0.001), fatigue (56.7% to 26.7%, p=0.018), Constipation (40.0% to 6.7%, p=0.006), Cold intolerance (26.7% to 6.7%, p=0.083), Irregularities of menstruation (51.7% to 24.1%, p=0.047). Hoarseness of voice (23.3% to 13.3%, p=0.505), Alopecia from (10.0% to 3.3%, p=0.605) which were not significantly changed. Out of 30 patients, at initial visit 1 (3.3%) patient had goiter and 4(13.3%) patients had present with oedema.

Table-II: Distribution of the study patients by clinical features of hypothyroidism before and after 3 months Levothyroxine replacement in hypothyroid patients (N=30)

Clinical features	Before treatment	After treatment	p-value
Weakness	22(73.3)	12 (40.0)	0.010[a]
Alopecia	3(10.0)	1 (3.3)	0.605[b]
Weight gain	17(56.7)	5(16.7)	0.001[b]
Cold intolerance	8(26.7)	2(6.7)	0.083[b]
Constipation	12(40.0)	2(6.7)	0.006[b]
Hoarseness of voice	7(23.3)	4(13.3)	0.505[b]
Fatigue depression	17(56.7)	8(26.7)	0.018[a]
Goiter	1(3.3)	1(3.3)	1.000[b]
Oedema	4(13.3)	2(6.7)	0.667[b]
Menstrual cycle (n=29)			
Regular	6(20.7)	14(48.3)	
Irregular	15(51.7)	7(24.1)	0.047[a]
Menopause	8(27.6)	8(27.6)	

p-value obtained by Chi-square test[(a)]and Fisher exact test[(b)]

Table-III showed the thyroid hormone profile of the study patients before and 3 months after treatment. Mean FT4 level at baseline and 3 months after treatment was significantly increased from 8.06±3.78 to 16.40±3.95 (p<0.001) and TSH level significantly reduced from 32.55±37.31 to 2.52±2.71 (p<0.001).

Table-III: Comparison of FT4 and TSH before and after 3 months Levothyroxine replacement in hypothyroid patients (N=30)

Hormone profile	Before treatment (Mean±SD)	After 3 months of treatment (Mean± SD)	p-value
FT4	8.06±3.78	16.40±3.95	<0.001[a]
Range (min-max)	(0.17-14.20)	(10.47-31.01)	
TSH	32.55±37.31	2.52±2.71	
Median	15.16	1.79	<0.001[b]
IQR	6.45-155.0	0.01-10.12	

p-value obtained by paired t-test[a] and Wilcoxon Signed Ranks Test[b]

Table-IV showed lipid parameters before and after levothyroxine replacement therapy for 3 months in hypothyroid patients. Mean Total cholesterol, TG, LDL-C level was significantly decreased from 193.27±41.69, 173.33±63.71, 119.58±40.11 to 177.80±38.17, 155.87±58.25, 103.07±26.25 (p=0.022, 0.044, 0.042) respectively. HDL-C before treatment was 45.04±13.14 and after treatment was 43.11±10.78 (p=0.415).

Table-IV: Comparison of lipid profile before and after 3 months Levothyroxine replacement in hypothyroid patients (N=30)

lipid profile	Before treatment (Mean±SD)	After 3 months of treatment (Mean± SD)	p-value
TC (mg/dl)	193.27±41.69 (137-336)	177.80±38.17 (102-281)	0.022
TG (mg/dl)	173.33±63.71 (60-312)	155.87±58.25 (59-311)	0.044
HDL (mg/dl)	45.04±13.14 (30-86)	43.11±10.78 (26-83)	0.415
LDL (mg/dl)	119.58±40.11 (75-236)	103.07±26.25 (61-161)	0.042

p-value obtained by paired t-test

Discussion:

This was a prospective analytic study done on 30 newly diagnosed hypothyroid patients. In the present study the mean age of the study patient was 35.40±11.52 years, minimum age was 19.0 and maximum age was 62.0. These results are near to the findings of a study that was done at center for Nuclear Medicine and ultrasound, Bogra medical college in 2007,[9] the mean age of hypothyroid patients was 35.59±6.91 years. Another study in Endocrine inpatient and outpatient departments of BIRDEM General Hospital from August 2013 to July 2014 and found mean age of the hypothyroid patients was 42.59±10.98 years.[10] A study done in Nepal in 2020 where the mean age of the patient was found 46.81 years.[11] In this study 6(20%) patients had positive family history of hypothyroidism, which was around similar to the study done in BSMMU from October 2015 to November 2016, in which showed that out of 154 cases 15(09.7%) patients had positive family history thyroid disorder.[12]We found that mean FT4 was low 8.06±3.78 and mean TSH was high 32.55±37.31 in hypothyroid patients which suggest that levothyroxine therapy was required and there was significantly increased FT4 16.40±3.95 and decreased TSH value 2.52±2.71 after thyroxine replacement. This result was consistent with previous studies conducted by Mir et al, that showed mean FT4 and TSH was 8.91±1.21 and 50.11±27.81 before treatment and after 6 months thyroxine replacement FT4 was 14.67±1.38 and TSH value was 2.93±1.08.[10] A study done by Raut et al, found that mean value of TSH was 12.09±1.89 and FT4 was 8.63±1.01 before therapy.[11] There was significant reduction in TSH value was 7.97±1.59 and mean FT4 was 7.11±1.16 which was not consistent with present study. In this study it was found that there was raised level of serum Total cholesterol, TG, LDL-C and HDL-C was normal in range at initial visit. After 3 months treatment with levothyroxine, total cholesterol, TG, LDL-C were reduced significantly, and HDL also reduced which was not statistically significant. Mean value of serum TC, TG, LDL-C and HDL-C before therapy were 193.27±41.69, 173.33±63.71, 119.58±40.11 and 45.04±13.14 and after levothyroxine replacement were 177.80±38.17, 155.87±58.25, 103.07±26.25 and 43.11±10.78 respectively. This result was consistent with many previous studies. The study of Mir et al reported that mean value of TC, TG, LDL-C, HDL-C at baseline and 6 months after treatment changes from 194.74±19.80, 242.96±62.79, 148.64±15.24, 32.20±3.28 to 163.49±17.69, 210.17±56.27, 114.66±12.52, 32.39±2.75 in primary hypothyroid patient.[10] There was significant reduction in mean TG, TC, LDL-C with less significant alteration in the level of HDL after replacement therapy with levothyroxine in the study of Raut et al[11] Pearce et al (2012) observed increased in serum TG, TC, LDL-C in subclinical hypothyroid patients which support present findings and the reason behind the raised TC, LDL-C may be due to increased formation of oxidized LDL-C leading to enhanced risk of atherosclerosis.[12] Monzani et al (2004), reported that in SCH patients after levothyroxine replacement therapy significantly reduced both TC (214.2±37.5mg/dl vs 191.63±2.5mg/dl), and LDL-C (138.9±32.3mg/dl vs 119.2±27.8mg/dl).[13] There was a reduction in the TG levels (94.0±31.9

mg/dl vs 88.1±30 mg/dl) which correlate with present study. However, in contrast to present observation, these authors reported a decline in HDL-C levels (56.5±11.7 vs 54.7±7.4). Contrary findings with regard to TG levels have also been reported by few of these authors. Ineck et al and Meier et aldid not observe any change in TG levels following levothyroxine replacement therapy.[14,15] Efstathiadou et alobserved no significant changes in serum lipid profile after levothyroxine therapy in SCH patient, which was contrary to present findings except for a decrease in HDL-C (59±15 to 55±14, p10μU/ml) and greater initial cholesterol level.[16] In this study the dose has been prescribed based on the level of TSH from 25, 50, 75, to 100 micrograms once a day and dose was adjusted after 4-6weeks. After 2-3 months of levothyroxine replacement serum TSH level was rechecked with the aim of keeping TSH in the lower half of recommended range (0.35-5.5μIU/mL).

Limitations:
The study was limited by a short duration, small sample size, and location in a tertiary hospital, and does not reflect the picture of the entire country.

Conclusion:
Early management of elevated TSH levels is crucial. Thyroxine replacement therapy is effective in improving lipid profiles and enhancing overall quality of life. Levothyroxine specifically lowers total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and triglyceride (TG) levels, while it does not have a significant impact on high-density lipoprotein cholesterol (HDL-C).

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