

**A STUDY OF SYMPTOM SCORE AND LIPID PROFILE IN SUBCLINICAL HYPOTHYROIDISM BEFORE AND AFTER THYROXINE SUPPLEMENTATION**Polu Poina Sreenivasulu<sup>1</sup>, Allam Sudha Rani<sup>2</sup>, Bingi Pratap<sup>3</sup>**HOW TO CITE THIS ARTICLE:**

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**ABSTRACT:** Hypothyroidism is the most common form of thyroid disorder with a broad range of clinical spectrum. Sub clinical hypothyroidism (SH) is the mildest form of the disease in which a few if any non-specific symptoms and/or lipid abnormalities are present. The effect of SH on lipid profile is controversial.<sup>[1,2]</sup> Elevation of total and LDL cholesterol is observed. SH is associated with subtle abnormalities in myocardial contractility, depression, sub fertility and ovalutary dysfunction. Thyroid replacement in SH is associated with improvement in above mentioned symptoms. This study was carried out to analyse symptom score and lipid profile in patients with SH before and after treatment with L-thyroxine.

**KEYWORDS:** Subclinical hypothyroidism, lipids, L-thyroxine.

**INTRODUCTION:** SH is defined as normal free T3 and T4 with elevated Thyroid stimulating hormone (TSH). A variety of names like decreased thyroid reserve, asymptomatic thyroiditis, preclinical hypothyroidism, biochemical or compensated hypothyroidism are designated. It has high prevalence in general population, particularly in elderly. It progresses to overt hypothyroidism in in patients who have high TSH and antithyroid antibody titres at diagnosis.

SH is associated with elevated total cholesterol and LDL cholesterol compared to euthyroid patients. Undetected SH in pregnancy may adversely affect the neuropsychological development and survival of fetus and have higher association of hypertension and toxemia.

Thyroxine therapy improves physical activity. The longer the duration of thyroid failure, the more muscle dysfunction was demonstrated. Behavioral and psychiatric complaints have received considerable attention and in general T4 replacement therapy has been useful.<sup>[3]</sup> Benefits have included improved memory.<sup>[4,5]</sup> and enhanced response to antidepressant medications in patients with depression.<sup>[6]</sup> Panic disorder may be more common in patients with thyroid failure and it has a less favorable response to antidepressant agents.

**AIMS AND OBJECTIVES:**

1. To study symptom score and lipid profile in patients with subclinical hypothyroidism.
2. To study the effect of L-thyroxine supplementation therapy on symptom score and lipid profile at 6 weeks, 3 months and 6 months after therapy.

**MATERIALS AND METHODS:** Thirty newly diagnosed, untreated patients with SH attending the endocrine clinic of Government General Hospital Kurnool were enrolled for the study.

Thyroid function screening by estimation of total T4, T3 and TSH were carried in subjects with goiter or in those with doubtful or subtle symptoms of hypothyroidism. Those with TSH > 6 microU/ml with normal T3 and T4 were diagnosed to have SH.

**Inclusion Criteria:**

1. Hashimoto's thyroiditis.
2. Treated hyperthyroidism.
3. Hypothyroidism without optimal treatment.
4. Subjects treated with lithium, amiodarone, iodine, iodine containing medications.

**Exclusion Criteria:**

1. Recovery from non-thyroidal illness.
2. Non-compliance with thyroxine therapy.
3. CRF.
4. Primary adrenal failure.
5. High TSH levels as an artifact due to circulating heterophilic antibodies against thyrotropin.
6. Medications like metoclopramide, domperidone and other dopamine antagonists.

**Clinical Assessment:** A detailed history for symptoms and concurrent illness was recorded and a thorough physical examination was carried out. The observations were recorded in a separate proforma. Scores were given to the symptoms and signs elicited, as per the recommendations of Zulewski et al.<sup>[7]</sup> The patients had routine investigations for renal and liver functions, chest X-ray and electrocardiography.

**Thyroid function Tests:** Estimation of TSH was performed by immunoradiometric assay (IRMAK-9). Serum T3 and T4 estimated by radio immunoassay using kits RIAK-4/4A and RIAK- 5/5A from BARC, Bombay.

**Lipid Profile:** Total cholesterol, HDL-C, triglycerides were estimated by using enzymatic calorimetric methods. VLDL-C was calculated by dividing total triglycerides by 5. LDL-C was calculated by using following Friedwald equation,<sup>[8]</sup> when triglycerides were <400mg/dl.

$$\text{LDL-c} = \text{TC} - (\text{HDL-c} + \text{TG}/5)$$

When triglycerides are >400 mg/dl, LDL-c estimation was done by enzymatic calorimetric method.

**Treatment and follow Up:** Symptom score and base line lipid profile were performed at the time of entry into the study. After an informed consent, the patients were started on L-thyroxine at substitutive doses, starting at 50mcg once daily. After 6 weeks of replacement therapy, the serum TSH estimation was repeated. If TSH was more than 6microU/ml, the dose L-thyroxine was increased to 75mcg/day or higher (Upto 125mcg/day). If TSH was less than micro U/m the dose of L-thyroxine was decreased to 25microg/day. The aim was to use a dose of thyroxine that will be sufficient to normalize TSH and not making symptom free. Follow up clinical evaluation repeat TSH, T3, T4 and lipid profile were performed at 6 weeks, 3 months and 6 months after dose the evaluation visit.

**Statistical Analysis:** The data were presented as mean + S. D. data of various estimations between 'before' and 'after' L-thyroxine therapy were compared by student's T test for paired data. A p value of <0.05 was considered stastically significant. Correlation between the various parameters and serum TSH was analysed using linear regression analysis.

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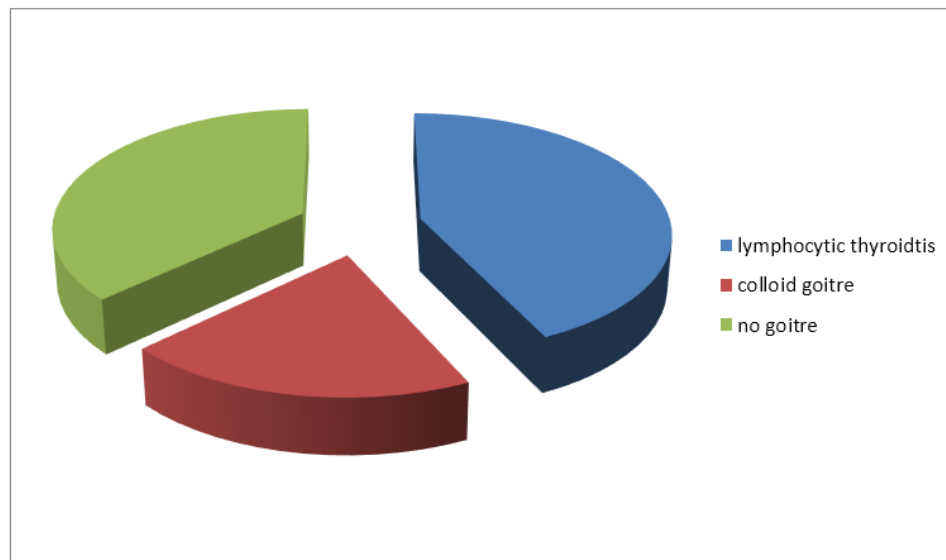
**Ethical Consideration:** No adverse effect was observed with the supplemental dose of L-thyroxine with the aim to normalize TSH. A detailed written consent was available from all the patients included in the study.

### RESULTS OF THE STUDY:

Age	N	%
10-19	1	3.3
20-29	5	16.7
30-39	9	30
40-49	11	36.7
50-59	2	6.6
60-69	2	6.6

**Table1: Age distribution**

Patients in the age group 30-49 years constituted major group (66.6%)



**Fig. 1: Causes of subclinical hypothyroidism in our study**

Symptoms	No. of patients
Diminished sweating	4(13%)
Hoarseness	6(20%)
Parasthesias	16(53%)
Dry skin	13(43%)
Constipation	8(26%)
Impairment of hearing	1(3%)

**Table 2: Distribution of symptoms in patients**

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Signs	No. of patients	%
Slow movements	0	0
Delayed ankle reflex	9	30
Coarse dry skin	12	40
Periorbital puffiness	18	60
Cold skin	2	7

Table 3: Distribution of signs

Each symptom and sign was given a score of 1 if present and a score of 0 if absent. 1 point is added to the sum of symptoms and signs in women considered as hypothyroid. A score of 3-5 is considered intermediate and  $< 3$  as euthyroid.

Score (points)	No. of patients
$<3$	13
3-5	7
$>5$	10

Table 4: Distribution of clinical scores

**Thyroid function tests:** Base line serum T3 T4 TSH was correlated with the clinical scores obtained by the patients with subclinical hypothyroidism. No significant correlation was noted ( $p > 0.05$ ).

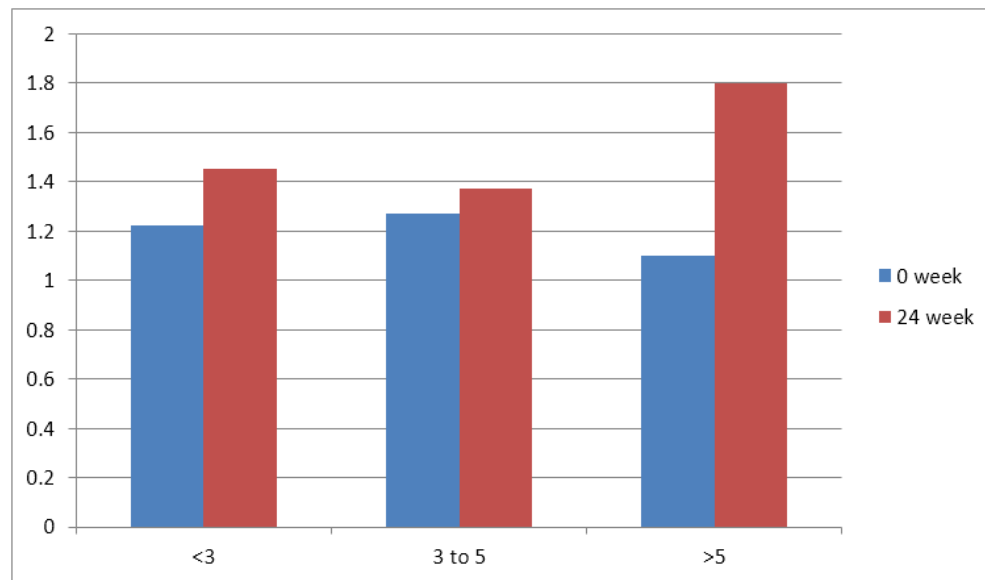
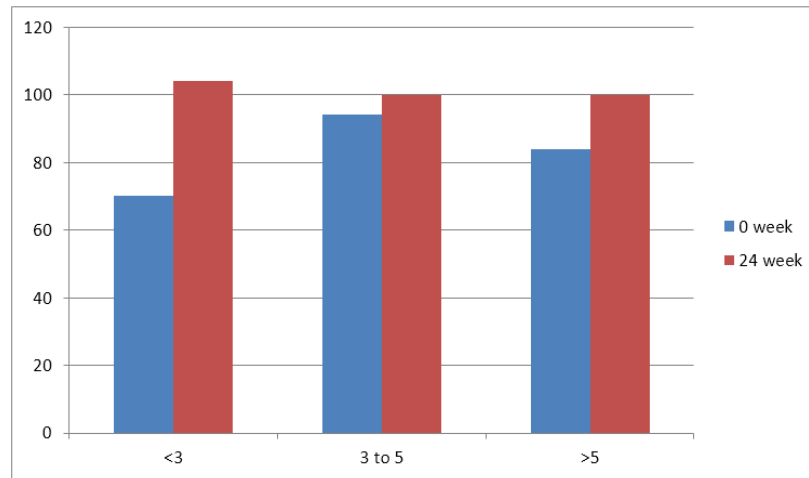
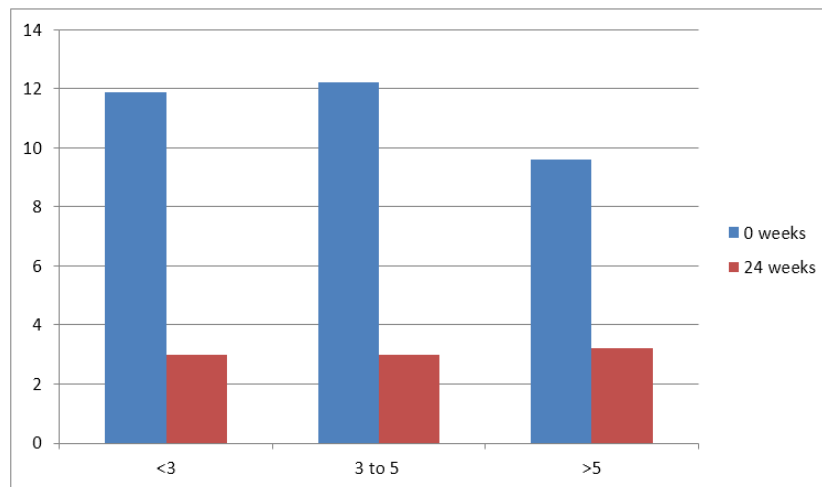


Fig. 2: Correlation of T3 with clinical scores before and after L-thyroxine therapy

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**Fig. 3: Correlation of T4 with clinical scores before and after L-thyroxine therapy**

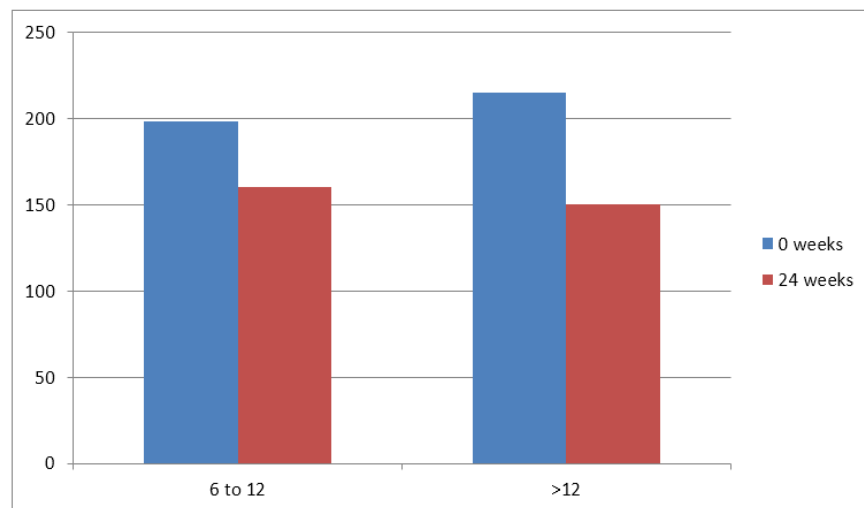


**Fig. 4: Correlation of TSH with clinical scores before and after L-thyroxine therapy**

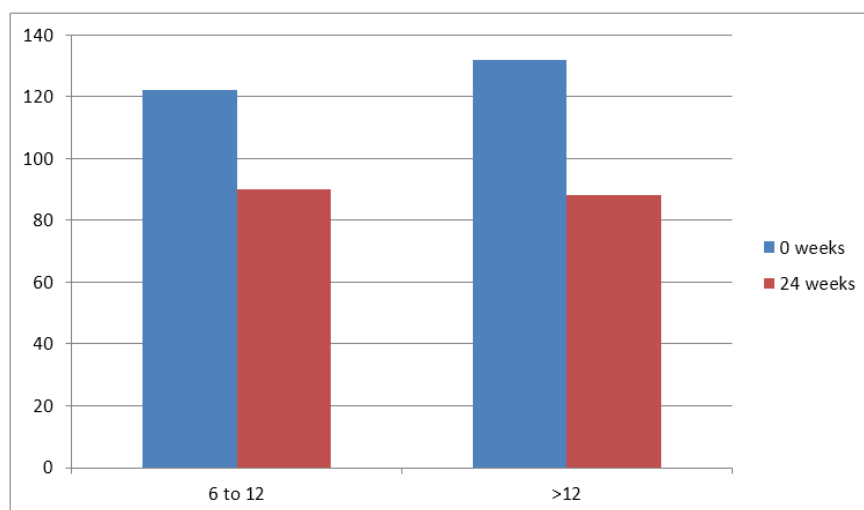
Lipid Profile	Total score <3(n=5)	Total score 3-5(n=15)	Total score >5 (n=10)
Total cholesterol	219	205	192
LDL-C	147	131.53	109.46
HDL-C	43.8	40.2	45.8
VLDL-C	30.88	30.46	32.31
TG	154.8	148.47	161.8

**Table 5: Total score and lipid profile before L-thyroxine therapy**

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**Fig. 5: Total cholesterol before and after L-Thyroxine therapy**



**Fig. 6: LDL cholesterol before and after L-Thyroxine therapy**

**DISCUSSION:** The issue whether subclinical hypothyroidism is simply a biochemical abnormality or a disease entity is debatable. The degree of impact of SH on target tissues is not clear. There was a female preponderance in our study (83.3%). This is in keeping with the reports on female gender bias published literature.

The mean age of our patients was 37.55+/- 10.08 years with in the range of 20-63 years. In the Wickham survey, which was a population based study in subjects with age of 18 years or more, SH was predominantly found in women of 54 years of age or more.<sup>[9]</sup> They constituted 31% of all women in whom SH was diagnosed. In our study population SH 86.8% of the patients were below 50 years of age, very similar to the age group reported in general population of western countries.

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Hundred percent of our patients had one or more symptoms. Weight gain and parasthesias were the most common symptoms found in our study. Coarse skin and periorbital puffiness were the predominant symptoms.

Autoimmune thyroiditis has been shown to be the most common cause of SH. Other causes include thyroidectomy, radio ablation of thyroid and drugs. In our study 19 patients (63%) had goiter. Lymphocytic thyroiditis was responsible for the goiter in 13 patients (68%) and 6 others (32%) had colloid goiter. No specific cause for SH could be found in 11 patients (37%).

Based on TSH levels SH divided into 3 grades. Grade I when serum TSH <6microU/ml. Grade II when serum TSH is 6-12 microU/ml and grade III when TSH >12microU/ml.

In our study significant decreases in total cholesterol and LDL-C. This was in accordance with Meier et al, who evaluating a double blind placebo controlled randomized trial showed that elevated serum lipids are lowered by thyroid hormone replacement in patients with mild thyroid failure. L-thyroxine therapy resulted in a decrease in mean serum cholesterol by 45.36 mg/dl (22.12%) and in LDL-C by 37.12% (29%) respectively. The results from the present study are in agreement with those of several uncontrolled intervention trials in the current literature.

Mild thyroid failure should be considered a risk factor to the development of atherosclerosis and coronary heart disease. A recently published population based study has given proven the same.<sup>[10]</sup> The mechanisms for this include hypercoagulable state and decreased endothelial effects of thyroid hormones.

In addition to changes in lipid profile significant improvement of clinical signs and symptoms of hypothyroidism assessed by clinical scores could be demonstrated. The results of the two controlled trials have shown clinical and metabolic improvements in patients with thyroid failure treated with thyroid hormones.<sup>[11,12]</sup>

Based on the observations we advise replacement of L-thyroxine in patients with mild thyroid failure and hypercholesterolemia particularly so in the presence of other cardiovascular risk factors. This reduces overall morbidity and mortality in SH.

### SUMMARY:

1. Patients with SH has female preponderance (83%).
2. Autoimmune etiology is the major cause (68%) of SH.
3. Most of them had one or more symptoms referable to hypothyroidism (100%). Majority of patients had grade II SH (63%).
4. There was significant improvement in clinical scores, 6 months after L-thyroxine therapy.
5. There was significant reduction in mean total cholesterol and mean LDL cholesterol 6 months after L-thyroxine therapy.

**CONCLUSION:** SH is often associated with abnormal lipid profile. L-thyroxine treatment sufficient to normalize TSH brings in symptomatic improvement, near normal lipid profile and there by imparts a better quality of life and perhaps lesser atherogenic risk.

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