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# Lipid Profile in Patients with Subclinical Hypothyroidism: A Prospective Case Control Study from a Tertiary Care Centre in North India

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**Original Research Article**

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**Abstract:** The epidemiological data of various lipid profile abnormalities in subclinical hypothyroidism in Jammu is scarce. In fact the entity of subclinical hypothyroidism is still not well recognized itself. We conducted a prospective case control study was conducted in the Department of Medicine, in Acharya Shri Chander College of Medical Sciences, Jammu, from November 2011 to October 2012. Lipid profile abnormalities of seventy patients with subclinical hypothyroidism were compared with 100 age and sex matched controls. Mean age of the patients with subclinical hypothyroidism was 38.83±11.60 years with a majority being females. The most common symptom in subclinical hypothyroid patients was easy fatigability present in 24.2% of the cases followed by weight gain in 14.3% and constipation in 12.8%. Mean TSH levels in cases with subclinical hypothyroidism was 9.16±2.99 µIU/ml. 47 patients (67%) with subclinical hypothyroidism had TSH ≤ 10 µIU/ml. 23 patients (33%) had TSH >10 µIU/ml. The mean serum triglyceride levels in cases was 146.37±31.50 mg/dl which was significantly higher than mean serum triglycerides of controls (133.85±25.43mg/dl) (p value=0.0048).Cases with subclinical hypothyroidism had a mean serum LDL-cholesterol value of 117.79±32.43 mg/dl as compared to euthyroid controls who had a mean serum LDL-cholesterol value of 93.69±25.06mg/dl. This was found to be statistically significant with a p value<0.0001. Cases with subclinical hypothyroidism had a mean serum HDL-cholesterol value of 36.93±6.89mg/dl as compared with euthyroid controls who had a mean serum HDL-cholesterol value of 38.30±8.17mg/dl. This was not statistically significant. The mean serum VLDL cholesterol value in cases was 29.31±6.45mg/dl which was significantly higher than controls (26.85±5.35mg/dl) (p value=0.0074). Subclinical hypothyroidism is most commonly found between the age group of 31-40 years. It is predominantly a disease of females. Subclinical hypothyroidism usually presents with non-specific symptoms like easy fatigability, weight gain, constipation etc. Subclinical hypothyroidism is associated with significant lipid abnormalities i.e., elevated serum total cholesterol, triglyceride, LDL-cholesterol and VLDL-cholesterol. The degree of dyslipidemia is directly related to the increase in TSH levels.

**Keywords:** Dyslipidemia, subclinical hypothyroidism.

## INTRODUCTION

Subclinical hypothyroidism was first described in the early 1970's after TSH estimation became routine. Subclinical hypothyroidism is defined as an elevated serum thyroid stimulating hormone (TSH) concentration in presence of normal serum free T4 and T3. The elevation of serum thyroid stimulating hormone levels reflects the sensitivity of the hypothalamic pituitary axis to small decreases in circulating thyroid hormone. In the progressive development of thyroid disease, abnormal values of serum TSH generally occur before there is diagnostic abnormality of serum T4, because of non- linearity of the negative feedback relationship between serum T4 and the release of TSH from the anterior pituitary. The term subclinical hypothyroidism suggests absence of symptoms and signs , however, nonspecific symptoms such as fatigue, weight gain, depressive feelings, lethargy, decreased appetite, cold intolerance, sleepiness, hair loss, muscle pain, constipation and mild cognitive disturbances (like poor ability to concentrate, poor memory etc) can be present. Based on previous population studies, the prevalence of subclinical hypothyroidism is about twice as common in women than men with a world-wide prevalence of 7.5%-8.5% in women and 2.8%-4.4% in men [1] **.** About 2% of pregnant women with high serum anti-thyroid antibody concentration develop subclinical hypothyroidism [2]. One of the most common causes of subclinical hypothyroidism is chronic autoimmune thyroiditis (Hashimoto's disease) which is commonly associated with increased titers of anti-thyroid antibodies such as anti-thyroid peroxidase and anti-thyroglobulin antibodies. This

disorder is suspected when thyroid enlargement is observed, but antithyroid antibodies may also be associated with atrophy of thyroid and hypothyroidism. Other frequent causes include treatment with ablative therapy of Grave's disease and inadequate thyroid hormone replacement therapy for overt hypothyroidism. History of neck irradiation, postpartum thyroiditis and certain autoimmune disorders (especially type 1 diabetes mellitus) also increase risk, as does the use of lithium or amiodarone, exposure to radiographic contrast agents and iodine deficiency. Thyroid hormones have significant effects on the synthesis, mobilization and metabolism of lipids [3]. The activity of malic enzyme and other lipogenic enzymes in the liver is related to the thyroid hormone status. In patients with full blown hypothyroidism, the serum levels of triglyceride total cholesterol, lipoprotein-a, Apo-B, Apo-A1 and LDL-cholesterol are elevated. There is reduction in hepatic lipase, cholesteryl ester transfer protein. Serum HDL concentrations are usually normal. In hypothyroidism, there will be reduction in the synthesis, mobilization and metabolism of lipids. As the lipogenic enzyme activity decreases the serum lipids tend to rise.

In patients with subclinical hypothyroidism, the same changes are present but are less marked and less consistent. The pattern of lipid abnormalities is important because it is a risk factor for atherosclerotic cardiovascular disease. Mean arterial blood pressure may be increased and cardiac output decreased in patients with subclinical hypothyroidism, but these effects can be reversed in patients with levothyroxine therapy. Studies have linked subclinical hypothyroidism to neuropsychiatric disease and have shown to be a risk factor for depression and mood disorders.

In the absence of definitive guidelines, some clinicians may elect to perform routine screening with serum TSH measurement or to measure serum TSH in patients with persistent non - specific complaints, especially women, elderly and persons with risk factors for thyroid failure. The Consensus Panel of the American Thyroid Association (ATA), American Association of Clinical Endocrinologists (AACE) and the Endocrine Society, recommend screening women who are pregnant or who wish to become pregnant if they have a personal or family history of thyroid disease, suggestive of signs or symptoms, type 1diabetes or an autoimmune disorder [4]. Measurement of serum TSH is generally considered the best screening test for thyroid disease. The test has been proved to be both sensitive and specific.

The indications for treatment of subclinical hypothyroidism are not established but general guidelines can be offered. Greater magnitude and duration of TSH elevation and high titers of anti-thyroid antibodies increase the probability that the condition will progress to overt hypothyroidism [5] and therefore increases the potential benefit of treatment with levothyroxine. There are conflicting reports on the effects of thyroid hormone replacement therapy on neuropsychiatric symptoms, serum LDL-C concentration and cardiac dysfunction [6]. It is justifiable to treat patients with serum TSH more than 10μIU/ml and those with positive anti-thyroid peroxidase antibody titers, because of an increased rate of progression to overt hypothyroidism. In patients with coronary artery disease and minimal elevation of serum TSH, however, it may be advisable to monitor the serum TSH level.

Overt hypothyroidism is associated with significant increases in circulating concentration of total and low density lipoprotein cholesterol [7], but it is uncertain, whether subclinical hypothyroidism with normal serum free T4 is also associated with hyperlipidemia. Some case-controlled studies [7], but not others [8] have reported increased concentrations of serum total cholesterol (TC) and low density lipoprotein cholesterol (LDL-C) in subjects with subclinical hypothyroidism compared with euthyroid controls. Several large cross-sectional studies found no significant difference in total cholesterol or LDL cholesterol between subjects with subclinical hypothyroidism and euthyroid subjects [9].

From this conflicting data in the randomized community surveys, one may question whether subclinical hypothyroidism is associated with dyslipidemia.

## MATERIALS AND METHODS

A prospective case control study was conducted in the Department of Medicine, in Acharya Shri Chander College of Medical Sciences, Jammu, from November 2011 to October 2012. Seventy (70) patients with subclinical hypothyroidism were taken into the study group and they were compared with 100 age and sex matched controls.

### Inclusion criteria

Patients fulfilling following criteria were included in the study:

- Elevated serum thyroid stimulating hormone (TSH) greater than 4.00 μIU/ml (normal range 0.4- 4.00 μIU/ml).
- Normal free T4 (0.89-1.76ng/dl) and normal free T3 (1.5-4.1 pg/ml).
- Asymptomatic patients or patients with nonspecific symptoms such as fatigue, weight gain, constipation, excessive sleep etc.

### Exclusion criteria

Patients with the following abnormalities were excluded from the study:

- Obese patients with BMI equal to or greater than 30Kg/m².
- Primary or secondary dyslipidemia.
- Smokers and alcoholics.
- Diabetes mellitus.
- Renal failure
- Hepatic failure.
- Diagnosed cases of hypothyroidism or those already on treatment.
- Patients with history of antipsychotic treatment or estrogen intake.

A detailed history was taken from all the patients and controls according to a pre-formed proforma. After an informed consent, all the patients and controls were subjected to a complete physical examination and following investigations: Complete Blood Count (CBC), Liver Function Test(LFT), Renal Function Test(RFT), Fasting Blood Glucose, Lipid Profile(TC, TG, LDL-C, HDL-C and VLDL)and Thyroid Function Test (serum TSH , free T4 and free T3).

Samples of lipid profile from patients and controls were taken after 12 hours of an overnight fast. Serum was separated from the blood by centrifugation at 3000 rpm. The levels of triglyceride and total cholesterol in serum samples were estimated by enzymatic calorimetric method on R XL Max auto-analyzer. The calibration will be carried out using quality control sera (bio-red). The levels of HDL-C in the serum will be estimated by phosphotungstic acid and magnesium chloride method, in which LDL-C, VLDL and chylomicrons get precipitated from the sera leaving HDL-C in the supernatant. The level of LDL-C and VLDL was calculated by Friedwald's formula:

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

(where TG/5 represents cholesterol contained in VLDL).

TSH, free T4 and free T3 were measured by chemiluminescence method on the Immulite 1000 analyzer machine.

**Table-1: Reference range of lipid profile**

| | |
|---|---|
| Total cholesterol | 50-200 mg/dl |
| Triglycerides | 30-150 mg/dl |
| LDL-cholesterol | 50-150 mg/dl |
| HDL-cholesterol | 35-65 mg/dl |
| VLDL-cholesterol | 10-30 mg/dl |

The Statistical Package for Social Sciences (SPSS) version 13.0 was utilized to analyze the results. For comparing the data of two groups based on ratio scale, a parametric test independent sample (student t-test) was used. For comparing of data based on nominal scale, chi-square test was used. P value of less than 0.05 was taken as statistically significant.

## RESULTS

A total of 70 cases and 100 controls were taken into the study. Those patients with subclinical hypothyroidism were taken as cases and euthyroid patients were taken as controls.

### AGE

Mean age of the patients with subclinical hypothyroidism was 38.83±11.60 years and that of controls was 40.06±13.32 years. Both groups were statistically similar with a p value = 0.53.

**Table-2: Distribution of cases in different age groups**

| Age (years) | No. Of cases | Percentage |
|---|---|---|
| 18-30 | 17 | 24.3 |
| 31-40 | 25 | 35.7 |
| 41-50 | 19 | 27.1 |
| 51-60 | 5 | 7.1 |
| 61-70 | 4 | 5.7 |
| Total | 70 | 100 |

**Table-3: Distribution of controls in different age groups**

| Age(years) | No. Of controls | Percentage |
|---|---|---|
| 18-30 | 32 | 32 |
| 31-40 | 24 | 24 |
| 41-50 | 22 | 22 |
| 51-60 | 12 | 12 |
| 61-70 | 10 | 10 |
| Total | 100 | 100 |

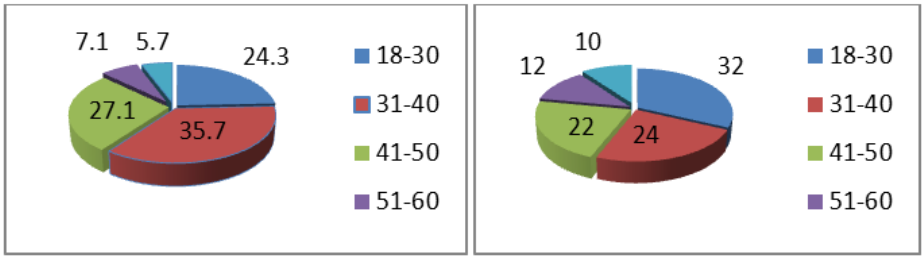


**Fig-1: (AGE) Cases Controls**

**Table-4: Sex distribution in cases**

| Sex | No | Percentage (%) |
|---|---|---|
| Male | 19 | 27 |
| Female | 51 | 73 |
| Total | 70 | 100 |

**Table-5: Sex distribution in controls**

| Sex | No | Percentage (%) |
|---|---|---|
| Male | 31 | 31 |
| Female | 69 | 69 |
| Total | 100 | 100 |

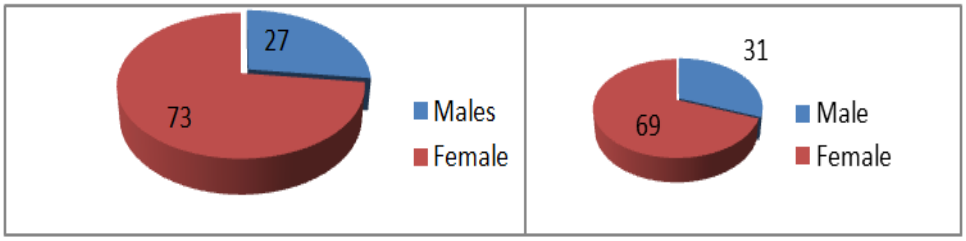


**Fig-2: (SEX) Cases Controls**

**SEX**

Out of 70 subclinical hypothyroid cases, 27% were males and 73% were females. While as in the control group 31% were males and 69% females.

**CLINIAL PRESENTATION**

The most common symptom in subclinical hypothyroid patients was easy fatigability present in 24.2% of the cases followed by weight gain in 14.3%, constipation in 12.8%, cold intolerance in 10%, menstrual abnormalities in 10%, dry skin in 8.5%, generalized body aches in 7.1%, excessive sleep in 5.7%, loss of appetite in 4.2%, primary infertility and forgetfulness in 1.4%.

**Table-6: Clinical presentation**

| Symptoms | No. Of patients | Percentage (%) |
|---|---|---|
| Easy fatigability | 17 | 24.2 |
| Weight gain | 10 | 14.3 |
| Constipation | 9 | 12.8 |
| Cold intolerance | 7 | 10 |
| Menstrual abnormalities | 7 | 10 |
| Dry skin | 6 | 8.5 |
| Generalized body aches | 5 | 7.1 |
| Excessive sleep | 4 | 5.7 |
| Loss of appetite | 3 | 4.2 |
| Primary infertility | 1 | 1.4 |
| Forgetfulness | 1 | 1.4 |

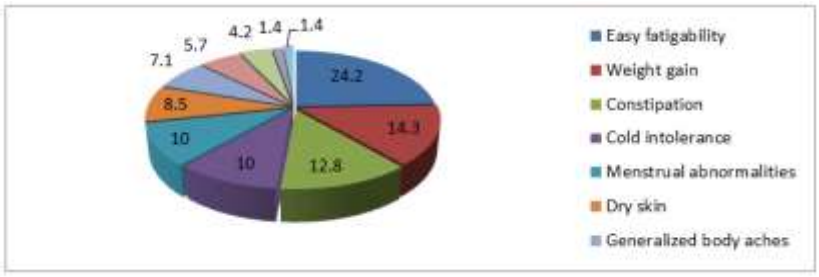


**Fig-3: Clinical presentation**

**TSH, (f) T3 AND (f) T4 LEVELS**

Mean TSH levels in cases with subclinical hypothyroidism was 9.16±2.99 µIU/ml. Euthyroid controls had a mean TSH level of 2.38±0.87 µIU/ml. This was found to be statistically significant with p value <0.001. Mean (f) T3 levels in cases was 2.23±0.44 pg/ml while the mean (f) T3 levels in controls was 2.33±0.41 pg/ml. Mean (f) T4 levels in cases was 1.18±0.20 ng/dl while the mean (f) T4 levels in controls was 1.21±0.24ng/dl. The mean (f) T3 and (f) T4 levels between cases and controls were not statistically significant.

**Table-7: Distribution of TSH, (f) T3 and (f) T4 levels in cases and controls**

| TSH, (f) T3, AND (f) T4 | Cases | Controls | P value |
|---|---|---|---|
| TSH | 9.16±2.99 | 2.38±0.87 | <0.0001 |
| (f) T3 | 2.23±0.44 | 2.33±0.41 | 0.13 |
| (f) T4 | 1.18±0.20 | 1.21±0.24 | 0.39 |

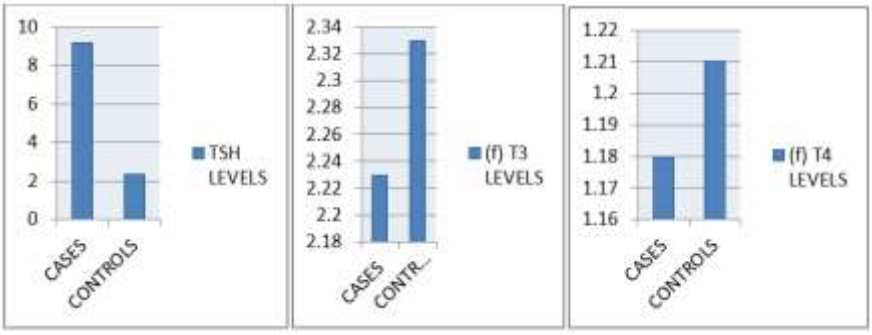


**Fig-4: TSH, (f) T3, (f) T4 Levels**

**Table-8: Distribution of cases with subclinical hypothyroidism**

| TSH | NO. | PERCENTAGE (%) |
|---|---|---|
| ≤10 | 47 | 67 |
| >10 | 23 | 33 |
| Total | 70 | 100 |

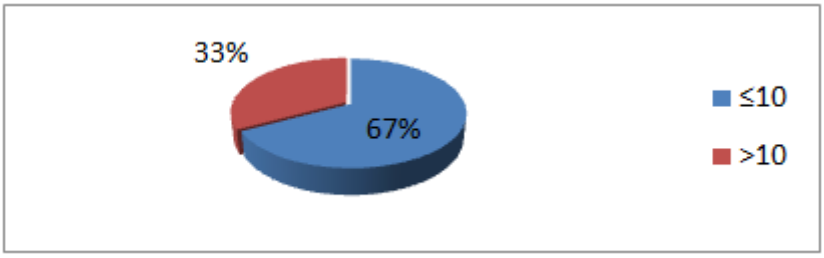


**Fig-5: Distribution of cases with subclinical hypothyroidism**

**Table-9: Relation between gender and serum TSH levels**

| GENDER | | TSH≤10µIU/ml | TSH>10µIU/ml | TOTAL |
|---|---|---|---|---|
| Male | N (%) | 11(57.9%) | 8(42.1%) | 19(100%) |
| Female | N (%) | 36(70.6%) | 15(29.4%) | 51(100%) |
| | TOTAL | 47(67.1%) | 23(32.9) | 70(100%) |

N = Number of patients

**DISTRIBUTION OF CASES**

47 patients (67%) with subclinical hypothyroidism had TSH ≤ 10 µIU/ml. 23 patients (33%) had TSH >10 µIU/ml.

**LIPID PROFILE**

The mean serum total cholesterol in cases with subclinical hypothyroidism (183.67±37.65 mg/dl) was significantly higher than mean serum total cholesterol of controls (159.44±28.28mg/dl) (p value< 0.0001).

The mean serum triglyceride levels in cases was 146.37±31.50 mg/dl which was significantly higher than mean serum triglycerides of controls (133.85±25.43mg/dl) (p value=0.0048).

Cases with subclinical hypothyroidism had a mean serum LDL-cholesterol value of 117.79±32.43 mg/dl as compared to euthyroid controls who had a mean serum LDL-cholesterol value of 93.69±25.06mg/dl. This was found to be statistically significant with a p value<0.0001.

Cases with subclinical hypothyroidism had a mean serum HDL-cholesterol value of 36.93±6.89mg/dl as compared with euthyroid controls who had a mean serum HDL-cholesterol value of 38.30±8.17mg/dl. This was not statistically significant.

The mean serum VLDL cholesterol value in cases was 29.31±6.45mg/dl which was significantly higher than controls (26.85±5.35mg/dl) (p value=0.0074).

**Table-10: Comparison of mean serum lipid profile between cases and controls**

| LIPID PARAMETERS Mean± SD (mg/dl) | CASES (N=70) | CONTROL (N=100) | P-VALUE |
|---|---|---|---|
| Total Cholesterol | 183.67±37.65 | 159.44±28.28 | <0.0001 |
| Triglyceride | 146.37±31.50 | 133.85±25.43 | 0.0048 |
| LDL-cholesterol | 117.79±32.43 | 93.69±25.06 | <0.0001 |
| HDL-cholesterol | 36.93±6.89 | 38.30±8.17 | 0.25 |
| VLDL | 29.31±6.45 | 26.85±5.35 | 0.0074 |

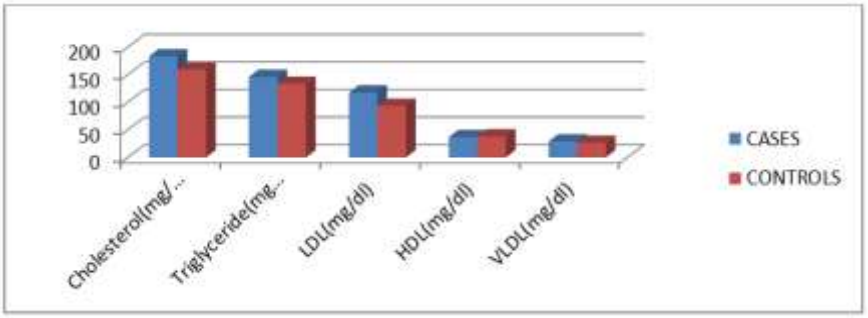


**Fig-6: Comparison of mean serum lipid profile between cases and controls**

**Table-11: Comparison of mean serum lipid profile between cases and controls in males**

| LIPID PARAMETERS Mean± SD(mg/dl) | CASES (N=19) | CONTROL (N=31) | P-VALUE |
|---|---|---|---|
| Total Cholesterol | 186.05±36.10 | 162.00±30.68 | 0.015 |
| Triglyceride | 154.68±35.51 | 134.63±21.44 | 0.016 |
| LDL-cholesterol | 117.44±32.51 | 94.58±27.16 | 0.01 |
| HDL-cholesterol | 35.11±7.59 | 39.84±9.42 | 0.07 |
| VLDL | 31.32±7.21 | 27.87±4.55 | 0.04 |

**LIPID PROFILE IN CASES AND CONTROLS ADJUSTED FOR SEX**

**MALE**

Mean concentration of serum total cholesterol (186.05±36.10 mg/dl), serum triglycerides (154.68±35.51 mg/dl), serum LDL-cholesterol (117.44±32.51 mg/dl), serum VLDL (31.22±7.21 mg/dl) was higher in male cases than controls.

**FEMALE**

Mean concentration of serum total cholesterol ((182.78±38.54 mg/dl) , serum triglycerides (142.59±29.67 mg/dl) , serum LDL-cholesterol(117.35±32.76 mg/dl) and serum VLDL(28.57±6.04 mg/dl) was higher in female cases than controls.

**Table-12: Comparison of mean serum lipid profile between cases and controls in females**

| LIPID PARAMETERS Mean± SD (mg/dl) | CASES (N=51) | CONTROL (N=69) | P-VALUE |
|---|---|---|---|
| Total Cholesterol | 182.78±38.54 | 157.21±27.17 | <0.0001 |
| Triglyceride | 142.59±29.67 | 130.38±25.04 | 0.016 |
| LDL-cholesterol | 117.35±32.76 | 92.86±24.22 | <0.0001 |
| HDL-cholesterol | 37.61±6.56 | 37.58±7.53 | 0.98 |
| VLDL | 28.57±6.04 | 26.19±5.39 | 0.025 |

**NUMBER OF CASES AND CONTROLS WITH LIPID PROFILE BEYOND NORMAL REFERENCE RANGE**

23(33%) cases of subclinical hypothyroidism had total cholesterol greater than 200mg/dl as compared to 7(7%) in the control group. Also greater percentage (40%) of cases with subclinical hypothyroidism had triglyceride levels greater than 150 mg/dl as compared to controls (17%). Higher percentage of cases with subclinical hypothyroidism had LDL-cholesterol greater than 150 mg/dl (19%) than controls (5%). HDL-cholesterol percentage was almost equal in the case and control groups (34% vs 33%). 25(36%) cases of subclinical hypothyroidism had VLDL levels greater than 30mg/dl as compared to 20 (20%) in the control group.

**Table-13: Number of cases and controls with serum lipid profile above reference range**

| ABNORMAL LIPID PROFILES | CASES (N=70) | | CONTROLS (N=100) | |
|---|---|---|---|---|
| | N | % | N | % |
| Total cholesterol (>200mg/dl) | 23 | 33 | 7 | 7 |
| Triglyceride (>150mg/dl) | 28 | 40 | 17 | 17 |
| LDL-cholesterol (>150mg/dl) | 13 | 19 | 5 | 5 |
| HDL-cholesterol (<35mg/dl) | 24 | 34 | 33 | 33 |
| VLDL (>30mg/dl) | 25 | 36 | 20 | 20 |

**LIPID PROFILE IN RELATION TO SERUM TSH**

Mean serum total cholesterol, triglyceride; LDL-cholesterol and VLDL cholesterol concentrations were higher in cases with serum TSH greater than10 µIU/ml than in cases with serum TSH equal or less than 10 µIU/ml and this difference achieved statistical significance. However, no relation was found between serum HDL-cholesterol and serum TSH levels.

**Table-14: Lipid profile in relation to TSH levels in cases**

| LIPID PARAMETERS Mean± SD (mg/dl) | TSH ≤10 µIU/ml | TSH > 10 µIU/ml | P VALUE |
|---|---|---|---|
| Total cholesterol | 168.38±29.71 | 214.96±32.85 | <0.0001 |
| Triglyceride | 136.04±24.33 | 167.48±34.35 | <0.0001 |
| LDL-cholesterol | 104.87±25.69 | 144.22±28.91 | <0.0001 |
| HDL-cholesterol | 37.05±7.15 | 36.70±6.46 | 0.84 |
| VLDL | 27.32±5.13 | 33.43±7.01 | <0.0001 |

## DISCUSSION

The nature and degree of dyslipidemia in overt hypothyroidism has been demonstrated in many studies. Overt hypothyroidism is associated with significant increase in total cholesterol and low density lipoprotein cholesterol. However, it is uncertain whether subclinical hypothyroidism is associated with dyslipidemia. The evidence provided by different authors remains controversial. There is growing evidence that subclinical hypothyroidism is an indicator of increased risk of atherosclerosis and myocardial infarction especially in women and the elderly.

The main aim of the present study was to identify patients with subclinical hypothyroidism and to determine the prevalence of dyslipidemia in these cases as compared to normal subjects. This was a case control study conducted over a period of one year from November 2011 to October 2012. Study included 70 patients with subclinical hypothyroidism and 100 age and sex matched control subjects. All cases had TSH >4.00 µIU/ml with normal range (f) T3 and (f) T4 levels. All controls had normal thyroid profiles.

In the present study the total number of patients with subclinical hypothyroidism who were studied was 70 which was quite similar to the number of patients with subclinical hypothyroidism taken in the study done by Efstatiadou et al who studied the lipid profile in 66 patients with subclinical hypothyroidism[10]. The age range of the study population was between 18 and 65 years which was quite similar to the age range considered by the study done by Kvetny *et al*., where the age range was between 20 and 69 years [11]. The mean age of patients with subclinical hypothyroidism was 38.83 years which was similar to the study done by Bandyopadhyay et al where the mean age was 38.56 years [12]. More number of cases were seen between the age group of 31-40 years.Of the 70 patients with subclinical hypothyroidism who were studied, 19 were males and 51 were females which corresponded to a percentage of 23% for males and 73 % for females. This was similar to the study by Bandyopadhyay et al where females constituted 78% of the study population [12].In the present study, the patients with subclinical hypothyroidism presented with non-specific symptoms among which the most common was easy fatigability (24.2%), followed by weight gain (14.3%), constipation (12.8%), cold intolerance (10%), menstrual abnormalities (10%), dry skin (8.5%), generalized body aches (7.1%), excessive sleep (5.7%), loss of appetite (4.2%), primary infertility (1.4%) and forgetfulness(1.4%). These results were similar to the ones published by Kung et al in which easy fatigability was the most common presenting symptom followed by weight gain [13]. Mean TSH values in our study was 9.16 µIU/ml which was similar to the study done by Kung et al. 67% of the cases had TSH ≤ 10 µIU/ml where as 33% had TSH values >10 µIU/ml. Mean (f) T3 and (f) T4 levels were 2.23 pg/ml and 1.18 ng/dl respectively which were within normal range but slightly less than controls and not statistically significant.A relation between dyslipidemia and atherosclerosis is well established in overt hypothyroidism. In a recent population based survey, subclinical hypothyroidism emerged as an independent risk factor for aortic atherosclerosis and myocardial infarction [14]. In a substantial number of studies, total cholesterol and LDL-cholesterol were significantly elevated in patients with subclinical hypothyroidism as compared to euthyroid controls [15,13,16]. Efstathiadou *et al*., found that patients with subclinical hypothyroidism had higher total cholesterol, LDL-cholesterol and apolipoprotein (a) and (b) levels compared to euthyroid controls [10]. The patients with high pretreatment total cholesterol showed significant reduction in both total cholesterol and LDL-cholesterol after thyroxine therapy but more pronounced reduction was found in patients with serum TSH > 10 µIU/ml. In the present study, a significant association was found to exist between subclinical hypothyroidism and dyslipidemia. The mean serum total cholesterol in patients with subclinical hypothyroidism was 183.67 mg/dl. This was statistically significant with a p value <0.0001. This was quite similar to the study done by Gupta et al who observed a mean total cholesterol of 192.13mg/dl [17]. However, many other studies have reported higher mean total cholesterol values as compared to this study. Efstathiadou *et al*., found a mean total cholesterol value 222mg/dl. Patients with subclinical hypothyroidism had a mean serum triglyceride value of 146.37 mg/dl, which was statistically significant as compared to controls with a p value =0.048. Kung et al have reported a mean triglyceride value of 159mg/dl [13].Mean LDL-cholesterol in patients with subclinical hypothyroidism was 117.79mg/dl with a statistically significant value of <0.0001 as compared to controls. These results were similar to the study done by Ravi Shekhar et al who found LDL-cholesterol to be statistically significant with a mean value of 118.1mg/dl. Efstathiadou *et al*., reported a mean LDL-cholesterol concentration of 139 mg/dl with statistical significance [10]. Rajan *et al*., in his study, observed a mean LDL-cholesterol of 134 mg/dl [18]. Patients with subclinical hypothyroidism had a mean serum HDL-cholesterol value of 36.93 mg/dl which was not statistically significant as compared to euthyroid controls. The study by Kung *et al*., has shown a mean HDL-cholesterol value of 39 mg/dl [13] while Rajan *et al*., observed a HDL-cholesterol value of 41.5 mg/dl which was not statistically significant [18]. The mean serum VLDL cholesterol value in patients with subclinical hypothyroidism was 29.31 mg/dl which was statistically significant as compared to controls with a p value =0.0074. As this was an indirect variable of serum triglycerides, studies have shown similar results as that in serum triglycerides.

In the present study, a significant association was found to exist between subclinical hypothyroidism and dyslipidemia. In the group as a whole, mean values of serum total cholesterol ($p<0.0001$), serum triglycerides ($p=0.048$), serum LDL-cholesterol ($p<0.0001$) were significantly elevated as compared to controls. These findings were consistent with the findings of Toruner *et al*., who in his study found that serum total cholesterol, triglycerides and LDL-cholesterol were higher in patients with subclinical hypothyroidism as compared to controls [19]. In the present study, there was no statistically significant difference between HDL-cholesterol values between patients with subclinical hypothyroidism and controls which was consistent with the findings of Cabral et al who observed no statistically significant difference between HDL-cholesterol values of cases as compared to controls while observing a significantly raised serum total cholesterol, triglyceride and LDL-cholesterol level [20].

Higher number of the cases (33%) of subclinical hypothyroidism had serum total cholesterol greater than 200mg/dl as compared to 7% in the control group.Also greater percentage (40%) of cases with subclinical hypothyroidism had triglyceride levels greater than 150 mg/dl as compared to controls (17%). Higher percentage of cases with subclinical hypothyroidism had LDL-cholesterol greater than 150 mg/dl (19%) than controls (5%). 36% cases of subclinical hypothyroidism had VLDL levels greater than 30mg/dl as compared to 20% in the control group. These findings were consistent with the study of Cabral *et al*., where greater number of patients with subclinical hypothyroidism had serum total cholesterol >200mg/dl and serum triglycerides >200mg/dl [20]. In the present study, serum total cholesterol, serum LDL-cholesterol and serum triglycerides were significantly higher in subclinical hypothyroid patients with serum TSH>10 µIU/ml than in patients with serum TSH less than or equal to 10 µIU/ml indicating that the degree of dyslipidemia is directly related to the rise in serum TSH levels. This finding was consistent with the findings of the study done by Duntas *et al*., who reported that the influence of subclinical hypothyroidism on lipids is directly proportional to the degree of serum TSH elevation. There is growing evidence that subclinical hypothyroidism is associated with dyslipidemia which itself results in an increased risk of atherosclerosis and myocardial infarction in patients especially women and the elderly.

## CONCLUSIONS

- Subclinical hypothyroidism is most commonly found between the age group of 31-40 years.
- It is predominantly a disease of females.
- Subclinical hypothyroidism usually presents with non-specific symptoms like easy fatigability, weight gain, constipation etc.
- Subclinical hypothyroidism is associated with significant lipid abnormalities i.e., elevated serum total cholesterol, triglyceride, LDL-cholesterol and VLDL-cholesterol.
- The degree of dyslipidemia is directly related to the increase in TSH levels.

## REFERENCES

1. Tunbridge WM, Evered DC, Hall R, Appleton D, Brewis M, Clark F, Evans JG, Young E, Bird T, Smith PA. The spectrum of thyroid disease in a community: the Whickham survey. Clinical endocrinology. 1977 Dec 1;7(6):481-93.
2. Klein RZ, Haddow JE, Falx JD, Brown RS, Hermos RJ, Pulkkinen A, Mitchell ML. Prevalence of thyroid deficiency in pregnant women. Clinical endocrinology. 1991 Jul 1;35(1):41-6.
3. Cappola AR, Ladenson PW. Hypothyroidism and atherosclerosis. The Journal of Clinical Endocrinology & Metabolism. 2003 Jun 1;88(6):2438-44.
4. Surks MI, Ortiz E, Daniels GH, Sawin CT, Col NF, Cobin RH, Franklyn JA, Hershman JM, Burman KD, Denke MA, Gorman C. Subclinical thyroid disease: scientific review and guidelines for diagnosis and management. Jama. 2004 Jan 14;291(2):228-38.
5. Rosenthal, MJ, Hunt, WC, Garry, PJ, Goodwin, JS. Thyroid failure in the elderly. Microsomal antibodies as discriminant for therapy. JAMA 1987; 258:209.
6. Karlin NJ, Weintraub N, Chopra IJ. Current controversies in endocrinology: screening of asymptomatic elderly for subclinical hypothyroidism. Journal of American Medical Directors Association 2004 September-October; 5(5): 333-6.
7. O'Brein T, Dinneen SF, O'Brein PC, Palumbo PJ. Hyperlipidemia in patients with primary and secondary hypothyroidism. Mayo Clinic's Proceeding 1993; 68: 860-6.
8. Muller B, Tsakiris DA, Roth CB, Gugliemetti M, Staub JJ, Marbet Ga. Haemostatic profile in hypothyroidism as potential risk factor for vascular or thrombotic disease. European Journal of Clinical Investigation 2001; 31: 131-7.
9. Pirich C, Mullner M, Sinzinger H. Prevalence and relevance of thyroid dysfunction in 1992 cholesterol screening participants. Journal of Clinical Epidemiology 2000; 53:623-9.
10. Efstathiadou Z, Bitsis S, Milionis HJ, Kuikuvitis A, Bairaktari ET, Elisaf MS, Tsatsoulis A. Lipid profile in subclinical hypothyroidism: Is L-thyroxine substitution beneficial? European Journal of Endocrinology 2001; 145(6): 705-10.
11. Kvetny JP, Heldgard PE, Bladbjerg EM, Gram J. Subclinical hypothyroidism is associated with a low-grade inflammation, increased triglyceride levels and predicts cardiovascular disease in males

below 50 years. Clinical Endocrinology.2004, Vol. 61, No.2: 232.
12. Bandyopadhyay SK, Basu AK, Pal SK, Roy P, Chatrabarti S, Pathak HS, Murmu BK. A study on dyslipidemia in subclinical hypothyroidism. Journal of Indian Medical Association 2006; 104:622-6.
13. Kung AWC, Pang RWC, Janus ED. Elevated serum lipoprotein –a in subclinical hypothyroidism. Clinical Endocrinology 1995; 43: 445-9.
14. Hak AE, Pols HA Visser TJ, Drexhange HA, Hofman A and Witteman JC. Subclinical Hypothyroidism is an independent risk factor for atherosclerosis and myocardial infarction in elderly women: The Rotterdam study. Annals of Internal Medicine 2000; 132:270-8.
15. Miura S, Itaika M, Yoshimura H, Kitahama S, Fukasawa N, Kawakami Y. Disturbed lipid metabolism in patients with subclinical hypothyroidism: Effect of L-thyroxine therapy. Internal Medline 1994; 33: 413-7.
16. Caraccino N, Ferrannini E and Monzani F. Lipoprotein profile in subclinical hypothyroidism: Response to levothyroxine replacement, a randomized placebo –controlled study. Journal of Clinical Endocrinology and Metabolism 2002; 87: 1533-8.
17. Gupta A, Sinha RS. Echocardiographic changes and alterations in lipid profile in cases of subclinical and overt hypothyroidism. JAPI 1996; 44 (8): 546, 551.
18. Rajan et al. Lipid profile changes in subclinical and overt hypothyroidism. APICON 2003. Poster session abstract.
19. Toruner F, Altinova AE, Karakoc A, Yetkin I, Ayvaz G, Cakir N, Arslan M. The relationship between subclinical hypothyroidism and cardiovascular disease. Advances on Therapy 2008; 25(5): 430-7.
20. Cabral MD, Costa AJ, Santos M, Vaisman M. Lipid profile alterations in subclinical hypothyroidism. The endocrinologist. 2004 May 1;14(3):121-5.