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# Association of Sub-Clinical Hypothyroidism with Abnormal Levels of Lipid in the Population of Nawabshah, Pakistan

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***Authors' contributions***

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

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## ABSTRACT

**Aims:** Aim of this investigation was to access the association of dyslipidemia with subclinical hypothyroidism.
**Methodology:** In this cross-sectional investigation, 1948 participants were recruited. Two groups were made; participants up to 18 years were in group A and Subjects over 18 years were incorporated in group 2. They were subdivided into control, subclinical hypothyroid 1, and subclinical hypothyroid 2. SPSS 21 was used for data analysis.
**Results:** Data of 1619 individuals were analyzed. The mean age of Group A participants was 12.79 ± 2.779, and the mean age of Group B participants was 42.58 ± 18.012. The prevalence of subclinical hypothyroid was found at 13.5 %. Significant differences have been observed while comparing Group A and Group B (P <0.001). Free tetraiodothyronine and Free triiodothyronine also

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showed a significant difference in both groups. (P<0.05). No significant difference between mean Thyroid-stimulating hormone levels was observed (P>0.05). No significant association between Controls and High-density Lipid values was found between Controls and subclinical hypothyroid.
**Conclusion:** We conclude that subclinical hypothyroidism leads to increased dyslipidemia. Lower Serum total cholesterol and low-density lipid levels were detected among children and participants under the age of 18 with Thyroid-stimulating hormone greater than 10 mIU/L. Thyroid-stimulating hormone less than 10.0 mIU/L had no lipid abnormalities in subclinical hypothyroid participants.

*Keywords: Dyslipidemia; HDL; LDL; sub clinical hypothyroidism.*

## 1. INTRODUCTION

The role of Thyroid hormones in lipid production, metabolism, and mobilization, is well documented, and primary hypothyroidism is associated with lipid abnormalities [1]. In people with subclinical hypothyroidism (SCH), numerous researchers have discovered a noteworthy raised in total cholesterol (TC) and low-density lipoprotein cholesterol (LDL) [2,3]. Even in euthyroid people, a link between TC and serum thyroid-stimulating hormone (TSH) has been uncovered [4].

The majority of the time, subclinical hypothyroidism has no symptoms. When symptoms do appear, they are usually nonspecific and widespread, such as anxiety, insomnia, lethargy, goitre, weight gain, loss of hair, and temperature intolerance [5]. Research suggests that untreated higher TSH levels can lead to hypertension and excessive cholesterol levels. In a study of older men and women, individuals with a blood TSH level of 7 mIU/L or more were twice as likely as those with a normal TSH level to develop congestive heart failure [6]. Because of its link to lipid problems, some doctors recommend treating subclinical hypothyroidism with thyroxine supplementation even if TSH readings are less than 10 mIU/L [7]. However, the outcome of thyroxine replacement on total cholesterol in subclinical hypothyroidism patients is debatable [8]. One more complication is discussed in a study that the rate of spontaneous abortion in pregnant women with Subclinical Hypothyroidism rises in early pregnancy [9]. Whether hyperthyroidism or hypothyroidism, Thyroid disease has been linked to coagulation issues [10]. Changes in circulatory hemodynamics, anomalies in diastolic function, endothelial dysfunction, hypercholesterolemia, and hyperhomocysteinemia are all associated with thyroid illness [11].

Studies have reported a high incidence of Cardio Vascular Disease (CVD) and other problems linked with Subclinical hypothyroidism. Thyroid function and lipid problems have not been linked in the population of Nawabshah, Sindh Pakistan, despite being predisposed to an atherogenic lipid profile. This research was conducted across multiple age groups to assess lipid irregularities in participants with subclinical hypothyroidism at various TSH levels in Nawabshah, Sindh, Pakistan.

## 2. METHODS AND MATERIALS

This study was conducted in the Department of Medicine, Peoples University of Medical and Health Sciences Nawabshah Pakistan between march 2020 to march 2021. The aim was to assess the general health of the local population, including school-going children, adults, and the elderly. Participation was voluntary. This study is a subset of the overall health assessment, including 1948 individuals.

In this study, individuals having a history of diabetes mellitus or fasting blood sugar level of > 5.6 mmol/L, Cardiac, hepatobiliary, kidney or thyroid disease, alcoholism, or taking lipid-lowering medications were excluded. Thus 329 subjects were removed from the initial database). The remaining subjects (n=1619) were separated into two groups: Group-A (children and Teenagers less than or up to 18 years) and Group-B (adults; Over 18 years of age) and were evaluated clinically, biochemically, hormonally, and immunologically.

After getting the Informed consent, we performed some tests, including Thyroid function tests (triiodothyronine T3 and tetraiodothyronine T4) and serum-TSH. Furthermore, we also analyzed the anti-thyroid peroxidase (TPO) antibodies on serum samples.

Thyroid function tests (TFTs) were performed using the radioimmunoassay (RIA) technique in children and adolescents and the electrochemiluminescence (ECL) assay in adults.

The typical ranges as stated by kit manufacturers are for Free triiodothyronine (FT3) (2.5–5.8 pmol/L), for Free tetraiodothyronine (FT4) is (11.5– 23 pmol/L), and for thyroid-stimulating hormone. For radioimmunoassay, it is in the range of 0.5–5.2 mIU/L. And for ECL kits its 2.8–7.1 mol/L for FT3, 12.0– 22.0 pmol/L for FT4, and TSH. Its range is 0.27–4.20 mIU/L. Anti-TPO antibody levels were determined using Roche (Germany) ECL kits, with a typical range of 0.0–34.0 IU/L. Anti-TPO antibody positivity was defined as a value of > 34.0 IU/L in subjects. Lipid estimates were performed using a fully automated biochemistry analyzer .The standardized ranges for LDL < 2.59 mmol/L, serum triglycerides (TG) > 1.70 mmol/L), HDL <1.04 mmol/L), and Serum TC (2.85–5.95 mmol/L).

We further divided the 2 groups in to 3 subcategories. In the control group i.e., Group A, subjects with Normal thyroid function test, In Group B, Individuals with SCH with normal FT4 and TSH ≤ 10.0 mIU/L, and in Group C, SCH subjects with normal FT4 and TSH greater than 10mIU/L were included.

SPSS 21 was used for data analysis. To check the normality of the data, we executed Shapiro–Wilk test. Data were reported as mean SD or number (percent) unless otherwise stated. We executed Chi-Square and student's t-test as well. A statistically significant p-value of 0.05 was used.

## 3. RESULTS

Analyzed data showed 1009 (62.32%) individuals in Group A and 610 (37.67%) individuals in Group B. We found that the mean age of Group A participants was 12.79 ± 2.779, and the mean age of Group B participants was 42.58 ± 18.012. A significant difference in the age group has been observed (P< 0.001). We had 515 (51.04%) males, and 494 (48.95%) females in group A. In Group B number of females is much higher, i.e., 384 (62.95%) and males were 226 (37.04%). Significance difference among gender has been observed (P< 0.001) (Table1).

There were 1401 (86.53%) patients with regular functions of the thyroid gland, 197 (12.16%) with SCH-1, and 21 (1.3%) with SCH-2. The overall prevalence of Subclinical hypothyroidism was 13.58 percent Table 2.

We found a significant difference between Group A and Group B when comparing Serum cholesterol Levels, Serum triglycerides HDL, and LDL (P< 0.001). In Group A, which comprises individuals up to 18 years, Serum cholesterol, Serum triglycerides, and LDL were reported significantly higher than the Group B, which comprises individuals more than 18 years in age. However, HDL levels are significantly lower in Group B (P< 0.001) Table 3.

We evaluated that the mean FT3 level in Group A was 4.71± 0.79, and in Group B, it was recorded 4.72 ± 0.90. Similarly, the mean FT4 level of Group A was 15.89 ±2.19 and in Group B was 15.29 ± 1.98. A significant difference among both groups was observed (P <0.05). No significant difference between in mean TSH levels was observed (P>0.05) Table 4.

Distinct age groups were shown to have a different influence on lipid metrics as a result of the SCH-2 treatment. Group-A participants with SCH-2 had considerably low levels of HDL than

**Table 1. Demographic characteristics of the study participants**

| Variables | Group A | Group B | P-Value |
|---|---|---|---|
| Frequency (n=1619) | 1009 (62.32%) | 610 (37.67%) | |
| Mean Age | 12.79 ± 2.779 | 42.58 ± 18.012 | < 0.001 |
| **Gender** | | | |
| Male | 515 (51.04%) | 226 (37.04%) | < 0.001 |
| Females | 494 (48.95%) | 384 (62.95%) | |

**Table 2. Frequency of subclinical hypothyroidism in both groups**

| Parameters | Group A (N=1009) | Group B (N=610) | Total (N=1619) |
|---|---|---|---|
| SCH-1 | 85 (8.42%) | 112 (18.36%) | 197 (12.16%) |
| SCH-2 | 10 (1.09%) | 11 (1.80 %) | 21 (1.3%) |
| Total | 95 (5.92%) | 124 (7.65%) | 218 (13.5%) |

**Table 3. Biochemical levels in group A and group B**

| Test | Serum cholesterol mmol/L (Range; Median) | Serum triglycerides mmol/L (Range; Median) | HDL mmol/L (Range; Median) | LDL mmol/L (Range; Median) |
|---|---|---|---|---|
| **Group A** | 3.69 ± 0.44 *(2.09 –7.85;3.59) | 1.29 ± 0.36 * (0.70 – 5.01;1.32) | 1.16 ± 0.12 * (0.76–1.98;1.12) | 2.20 ± 0.36 * (1.14–4.51; 2.29) |
| **Group B** | 3.99 ± 0.79 * (2.35–7.38; 3.99) | 1.71 ± 0.54 * (1.04–4.92;1.589) | 1.123±0.20 * (0.62–1.59;1.09) | 2.46 ±0.59 * (1.31–4.81;2.41) |
| P-Value | < 0.001 | < 0.001 | < 0.001 | < 0.001 |

**Table 4. Levels of hormonal parameters in both groups**

| Hormonal parameters | Group A | Group B | P-Value |
|---|---|---|---|
| Mean FT3 (pmol/L) | 4.71± 0.79 | 4.72 ± 0.90 | < 0.023 |
| Mean FT4 (pmol/L) | 15.89 ±2.19 | 15.29 ± 1.98 | < 0.001 |
| Mean TSH (mIU/L) | 3.43 ± 3.205 | 3.46 ± 3.201 | > 0.75 |

**Table 5. Lipid levels (mmol/L) according to TFT in group A and group B**

| | Normal TFT | SCH-1 | SCH-2 | |
|---|---|---|---|---|
| **Group A** | **N=913** (89.59%) | **N=** 85 (8.42%) | **N=** 11 (1.09%) | **P-value** |
| S cholesterol | 3.70 ± 0.46 | 3.64 ± 0.45 | 4.11±0.74 | 0.89 ¶, 0.19 Ω, 0.26 Ɫ |
| S triglycerides | 1.09 ± 0.34 | 1.24 ± 0.27 | 1.41 ± 0.36 | 0.18 ¶, 0.31 Ω, 0.03 Ɫ |
| HDL | 1.14 ± 0.12 | 1.13 ± 0.10 | 1.07 ± 0.11 | 0.55 ¶ 0.001 Ω, 0.001 Ɫ |
| LDL | 2.23 ± 0.32 | 2.21 ± 0.30 | 2.44 ± 0.56 | 0.16 ¶,0.076 Ω , 0.035Ɫ |
| **Group B** | **N= 486** (79.67%) | **N=112** (18.36%) | **N= 12** (1.8%) | |
| S cholesterol | 4.06 ± 0.84 | 4.12 ± 1.0 | 4.33 ± 0.80 | 0.258 ¶ , 0.031 Ω, 0.009 Ɫ |
| S triglycerides | 1.53 ± 0.51 | 1.52 ± 0.57 | 1.40 ± 0.38 | 0.29 ¶ , 0.28 Ω, 0.083 Ɫ |
| HDL | 1.12 ± 0.17 | 1.14 ± 0.21 | 1.10 ± 0.14 | 0.24 ¶, 0.33 Ω,0.082 Ɫ |
| LDL | 2.44 ± 0.60 | 2.47 ± 0.63 | 2.80 ± 0.57 | 0.84 ¶ ,0.0001 Ω, 0.0001Ɫ |

¶ P-value between individuals with Normal TFT and SCH-1.
**Ω** P-value between individuals with Normal TFT and SCH-2.
**Ɫ** P-value between individuals with SCH-1 and SCH-2.

the controls and SCH-1 subjects, and this was the only lipid anomaly detected in this group. On the other hand, in adults (Group-B), TC and LDL were considerably higher in participants with SCH-2. However, we didn't find any significant association between reduced HDL levels compared to Controls and SCH1 (Table 5).

## 4. DISCUSSION

In the current study, we observed that Subclinical hypothyroidism leads to increased dyslipidemia. We also found that the occurrence of subclinical hypothyroidism was 13.5%, and it increased with age. TSH10 mIU/L was found in 90 percent of SCH patients. Previous studies performed in different parts of the world and on different populations reported that the prevalence of SCH is in the range of 3-15% [12-14]. A study performed in Jinnah Postgraduate Medical Centre, Karachi, reported 62.05% of patients were diagnosed with thyroid disorders, whereas 260 9.42% patients had SCH [15] A recent study performed in Hyderabad, Sindh, Pakistan also reported the same findings [16]. Data from the United States of America reported that around 10.6% of the population suffers from hypothyroidism [17]. Higher total cholesterol and low-density lipoprotein cholesterol, primarily due to reduced katabolism and turnover, have been linked to raised pathology and death from CVD in overt hypothyroidism [18]. However, due to the limited studies and inconsistent results, the association between sub-clinical hyperthyroidism, CVD, and serum lipid levels remains somewhat ambiguous [19,20]. Though there is controversy about the impact of thyroxine replacement therapy on lipid levels in SCH patients [21], there are guidelines for treating SCH patients with dyslipidemia with TSHb10 mIU/L [7].

Hypothyroidism is also associated with lipid imbalances, which lead to atherosclerosis. Thyroid hormones and their substrates promote the utilisation of lipids and lipid molecules in hypothyroid patients, resulting in increased mobility of stored triglycerides in adipose tissue. Clinical hypothyroidism has been associated to a number of cardiovascular diseases, including with hypertension and hypercholesterolemia [22].

When equating SCH-2 and other sub-groups, the only considerable variation in lipid markers in Group A was found in HDL levels. In Group-A, there was no variance in the frequency of the individuals with abnormal levels of lipid between SCH-1 and controls, nor between SCH-2 and controls. Similar findings were reported in previous studies performed in Asia and Europe [23,24]. In Group B, where all participants were over 18 years old, there was no significant difference in lipid levels or the prevalence of lipid abnormalities between SCH-1 individuals and controls. This is in line with a previous study that found no change in the cardiovascular risk profile of old age individuals and people in their mid ages with mild SCH and regular thyroid gland function [25]. A study performed in Japan with a considerable sample size reported no relationship between subclinical hypothyroidism and lipid levels [26]. While comparing controls and SCH-1 participants, TC and LDL became considerably greater in SCH-2 subjects. Others have discovered that patients with TSH > 10 mIU/L have higher TC levels [27]. In a recent study, researchers found a link between age, TSH, LDL, and carotid intima medium thickness (CIMT) in SCH patients [28]. FT3 and FT4 were shown to be adversely linked with serum cholesterol and LDL, as previously observed in both subclinical hypothyroidism and euthyroid people [29]. Systemic autoimmune disorders have been linked to significant changes in lipid parameters and metabolism [30]. Anti-TPO antibody-positive euthyroid patients had considerably greater serum TC and LDL than those lacking anti-TPO antibodies [31,32]. Thyroid autoimmunity did not affect baseline lipid profile in one small case-control study [33].

Further and extensive studies are required in this domain to find out the impact and effects of SCH.

## 5. CONCLUSIONS

We conclude that subclinical hypothyroidism leads to increased dyslipidemia. Low HDL levels were found in children and teenagers below 18 years with TSH greater than 10 mIU/L, while higher TC and LDL levels were found in adults with TSH equal to 10 mIU/L. There were no lipid abnormalities in SCH participants with TSH less than 10.0 mIU/L.

## CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

## ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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