Original Research Article

Association of Sub-Clinical Hypothyroidism with abnormal levels of lipid in the population of Nawabshah, Pakistan

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 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:

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.

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]. 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 [5]. However, the outcome of thyroxine replacement on total cholesterol in subclinical hypothyroidism patients is debatable [6]. Thyroid function and lipid problems have not been linked in the population of Hyderabad, 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.

Methods and materials

This study was conducted in 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. The participation was voluntary. This study is a subset of the overall health assessment, which included 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. 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.

Lipid estimates were performed using a fully automated biochemistry analyzer (NAME OF THE MACHINE). 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),

Those individuals who had the following abnormalities were recruited in Groups A (Dyslipidemia):

TG > 1.70 mmol/L, High-density lipoprotein cholesterol < 1.04 mmol/L, TC > 5.18 mmol/L, or low-density lipoprotein cholesterol > 3.37 mmol/L [7]. The cut offs for defining dyslipidemia in Group-2 subjects were: TC > 6.21mmol/L, serum TG > 1. 70mmol/L, HDL < 1.04 mmol/L in males and < 1.3 mmol/L in females, or LDL > 4.14 mmol/L [8]

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.

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

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)**

Table 1: Demographic Characteristics of the Study Participants.

Variable	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%)	

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**

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%)

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**

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

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**

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

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 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).**

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 Ɐ
S triglycerides	1.09 ± 0.34	1.24 ± 0.27	1.41 ± 0.36	0.18 ¶, 0.31 Ω, 0.03 Ɐ
HDL	1.14 ± 0.12	1.13 ± 0.10	1.07 ± 0.11	0.55 ¶ 0.001 Ω, 0.001 Ɐ
LDL	2.23 ± 0.32	2.21 ± 0.30	2.44 ± 0.56	0.16 ¶,0.076 Ω , 0.035Ɐ
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 Ɐ
S triglycerides	1.53 ± 0.51	1.52 ± 0.57	1.40 ± 0.38	0.29 ¶ , 0.28 Ω, 0.083 Ɐ
HDL	1.12 ± 0.17	1.14 ± 0.21	1.10 ± 0.14	0.24 ¶, 0.33 Ω,0.082 Ɐ
LDL	2.44 ± 0.60	2.47 ± 0.63	2.80 ± 0.57	0.84 ¶ ,0.0001 Ω, 0.0001Ɐ

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

Discussion

In the current study, we 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%.[9-11]. 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. [12] A recent study performed in Hyderabad also reported the same findings. [13] Data from the United States of America reported around 10.6% of the population is suffering from hypothyroidism.[14] 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 [15]. However, due to the limited studies and inconsistent results, the association between sub-clinical hyperthyroidism, CVD, and serum lipid levels remains somewhat ambiguous. [16, 17] Though there is controversy about the impact of thyroxine replacement therapy on lipid levels in SCH patients [18], there are guidelines for treating SCH patients with dyslipidemia with TSHb10 mIU/L [5].

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.[19, 20] 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

[21]. A study performed in Japan with a considerable sample size reported no relationship between subclinical hypothyroidism and lipid levels [22]. 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 [23]. In a recent study, researchers found a link between age, TSH, LDL, and carotid intima medium thickness (CIMT) in SCH patients [24]. Serum TSH was shown to be positively connected with serum cholesterol level and low-density lipoproteins and showed a negative correlation with High-density lipoproteins in the current investigation, as shown by other researchers across a wide variety of ages groups and thyroid function levels [25]. FT3 and FT4 were shown to be adversely linked with serum cholesterol and LDL, as previously observed in both subclinical hypothyroidism and euthyroid people [26]. Systemic autoimmune disorders have been linked to significant changes in lipid parameters and metabolism [27]. Anti-TPO antibody-positive euthyroid patients had considerably greater serum TC and LDL than those lacking anti-TPO antibodies. Thyroid autoimmunity did not affect baseline lipid profile in one small case-control study [28].

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

Conclusions

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. Moreover, for participants with SCH-1 (TSH10.0 mIU/L) and accompanying lipid abnormalities, our findings advise against thyroxine treatment. A future study is needed to determine the effect of treating SCH with 10.0 mIU/L on lipid abnormalities.

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