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CORRELATION OF INTERLEUKIN-6 AND LIPID PROFILE WITH SUBCLINICAL HYPOTHYROIDISM

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Abstract

Background: Subclinical Hypothyroidism (SCH) is a common thyroid disorder that usually presents a few or no symptoms. It is defined by slight rise in Thyroid Stimulating Hormone (TSH) level (4.6-10.5 mIU/L), while T3 and T4 remain normal in SCH. Its global prevalence varies, with higher rates in India and among women. Interleukin-6 (IL-6) is an early marker of inflammation, linked to TSH stimulation and atherosclerosis development. Dyslipidaemia, defined by abnormal blood lipid levels, contributes to cardiovascular diseases. It involves elevated Triglycerides (TG) and Total Cholesterol levels (TC), alongside reduced High-Density lipoprotein (HDL). These conditions intertwine, impacting metabolic and immune responses, potentially leading to cardiovascular complications. This study aims to correlate between of Interleukin-6 (IL-6) and Lipid profile with Subclinical Hypothyroidism. **Material and methods**: To identify cases of SCH, the serum concentrations of TSH, Total Triiodothyronine (T3), and Thyroxine (T4) were estimated using an Enzyme Linked Immunosorbent Assay (ELISA) method. Serum IL-6 was performed using ELISA and lipid profile were estimated by using Semi autoanalyzer in this study. **Results**: SCH subjects have significantly higher Total cholesterol, Triglycerides, LDL, and IL-6 and decreased HDL with p-value ≤ 0.001. TSH levels are positively correlated with Total cholesterol (r = 0.492, p-value ≤ 0.001), Triglycerides (r = 0.488, p-value ≤0.001), LDL (r = 0.396, p-value ≤ 0.001), and inflammatory marker IL-6 (r = 0.480, p-value≤ 0.001). **Conclusion:** it is concluded that SCH increases inflammatory marker and lipid profile, making individuals more susceptible to cardiovascular disease. These findings emphasise the necessity of early SCH diagnosis and therapy to reduce CVD risk.

Keywords: Subclinical Hypothyroidism, Interleukin-6, Thyroid Stimulating Hormone, Dyslipidaemia.

INTRODUCTION

Subclinical Hypothyroidism (SCH) is a prevalent thyroid condition with few or no signs and symptoms resembling hypothyroidism. According to Indian Thyroid Society, SCH can be defined as condition, in which the levels of blood serum T3 and T4 are within the normal range, but there is a slight increase in the serum concentration of TSH, ranging from 4.5-10 mIU/L [1]. The global incidence of SCH exhibited variations based on factors such as gender, age, race, ethnicity, and geographic region, ranging from 0.4% to 16.9%. In India it is found to be between 9-11.4%, whereas in the adult population of northern India, it is around 10.25% [2,3,4]. The prevalence of SCH is more among females [5].

IL-6 is an early inflammatory marker of inflammation and it belongs to the T-helper-2(Th2) class of cytokines, playing a crucial role in humoral immune response [6]. IL-6

serves as a prominent and dependable indicator for quantifying the inflammatory reaction, leading to synthesis of CRP in the liver. Consequently, this indirectly stimulates the development of atherosclerosis. TSH induces the production of IL-6 by adipocytes in mature 3T3-L1 adipocytes, The activation of IL-6 gene transcription is achieved through TSH signalling by means of the cAMP-PKA pathway [7].

Dyslipidaemia is characterised by the presence of one or more of the specified factors in the blood: Triglyceride levels ≥ 130 mg/dL; Total cholesterol levels ≥ 200 mg/dL; low-density lipoprotein cholesterol levels ≥ 100 mg/dL; and high-density lipoprotein cholesterol levels ≤ 40 mg/dL. Dyslipidaemia is the main underlying factor responsible for the development of cardiac and metabolic disorders, such as atherosclerotic cardiovascular disease. This condition is characterised by elevated levels of TC, TG, and LDL-C, together with reduced level of HDL-C [8]. Hypothyroidism typically manifests as a progressive disorder that impacts every physiological process. Serum levels of Tumour Necrosis Factor-α (TNF-α) and Interleukin-6 (IL-6) increase, suggesting that hypothyroidism aggravates heart failure by influencing heart rate and blood pressure (BP) and increasing cardiovascular stiffness and cardiomegaly dyslipidaemia inflammatory state [9].

MATERIALS AND METHODS

The study was carried out at the Department of Biochemistry, Central Research Laboratory, in collaboration with the Department of Medicine, SMS&R, Sharda University, Greater Noida, Uttar Pradesh. The study obtained permission from the Institutional Ethical Committee. The study was carried out as a cross-sectional study, encompassing a total of 100 patients who has been diagnosed with SCH.

Inclusion criteria:

Identified cases of SCH subjects between (18 to 60) years old, with TSH level between (4.6 and 10 mIU/L) and normal T3, and T4 levels

Exclusion Criteria:

Subjects under the age of 18 with subclinical hypothyroidism (SCH). Instances of pregnancy and other recognised endocrine issues, Individuals with concurrent medical illnesses such as Diabetes mellitus, cardiovascular disorders, and hypertension (high blood pressure), Women who are taking oral contraceptive pills, Issues regarding the use of drugs such as Glucocorticoids, Dopamine, and Levothyroxine.

Biochemical Analysis

Morning fasting 5 mL venous blood samples was collected from the selected Subjects. The serum was separated from whole blood using centrifugation machine at 3000 rpm for 20 minutes and the serum samples were stored at a temperature of -20°C. In order to estimate the levels of serum TSH, Total T4, Total T3 and Interleukin-6 ELISA was performed while Lipid Profile was assessed using the Semi Auto analyzer (star 21 plus).

Statistical Analysis

The analysis was conducted using SPSS version 22, which is a statistical software. A one-sample t-test has been used to calculate the result. A p-value ≤ 0.05 or less is considered statistically significant, while a p-value ≤ 0.001 or less is considered extremely statistically significant. To find the relationship between variables The

Pearson Correlation test has been implemented.

Observation And Results: In this study 100 subjects were enrolled out of which 78 were females and rest 25 were male as shown in fig.1. TC, TG, LDL, I-6 were significantly increased with (p-value ≤0.001) as shown in table no.4, 5,6, and 8. While HDL was significantly decreased with p-value (≤0.001) as shown in table no.7.TSH has positive significant correlation with Total cholesterol (r = 0.492) with (p-value ≤ 0.001), Triglycerides (r = 0.488) with (p-value ≤ 0.001), LDL (r = 0.396) with (p-value ≤ 0.001), Interleukin -6 (r = 0.480) with (p-value ≤ 0.001). TSH has non-significant correlation with HDL (r = 0.488) with (p-value ≤ 0.001) as shown in table 9 and 10.

Table 1: Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
AGE	100	19	60	37.90	11.50
tT3 (ng/ml)	100	.96	1.94	1.38	.20
tT4 (µg/ml)	100	5.41	10.60	8.22	1.43
TSH mIU/L	100	4.86	9.84	6.95	1.67
TC (mg/dl)	100	154.00	270.00	215.30	28.12
TG (mg/dl)	100	105.60	289.00	186.66	43.74
HDL(mg/dl)	100	13.12	49.38	29.94	8.14
LDL (mg/dl)	100	55.55	207.87	146.63	29.73
VLDL(mg/dl)	100	21.12	57.80	37.43	8.66
IL-6 (pg/ml)`	100	7.56	22.25	13.67	3.50

Gender Distribution:

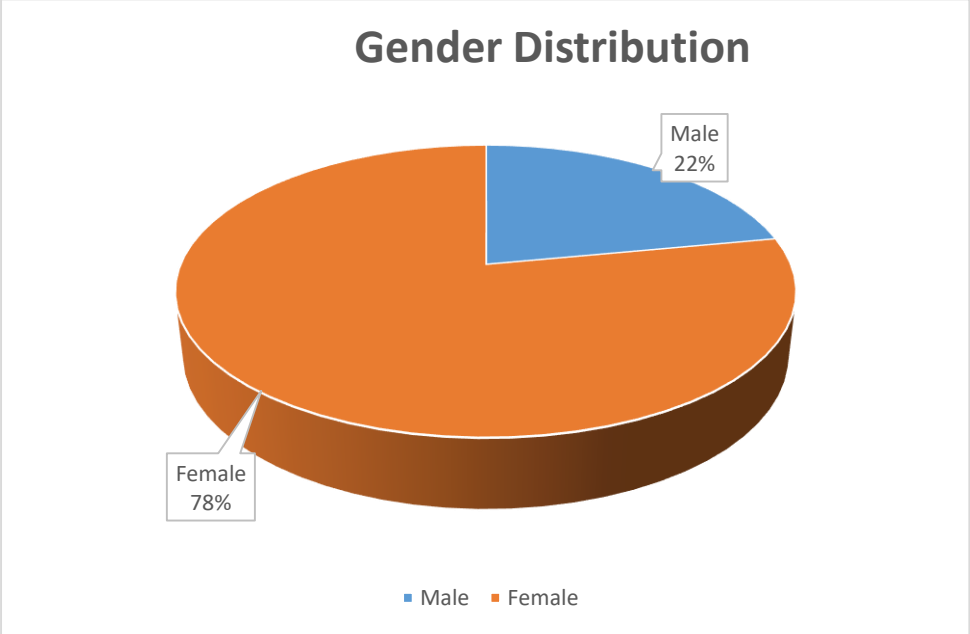

Figure 1: showing Gender Distribution of the study

This pie chart shows that 100 subjects were included in this study out of which 78 were Females and rest were Males.

Table 3: TSH level in SCH

One-Sample Test						
	Test Value = 10					
	t	df	Sig. (2-tailed)	Mean Difference	95% Confidence Interval of the Difference	
					Lower	Upper
TSH (mIU/L)	-18.273	99	.000	-3.05430	-3.3860	-2.7226

Table 4: TC level in SCH

One-Sample Test						
	Test Value = 200					
	t	df	Sig. (2-tailed)	Mean Difference	95% Confidence Interval of the Difference	
					Lower	Upper
TC (mg/dl)	5.440	99	.000	15.30000	9.7195	20. 8805

Table 5: TG level in SCH

One-Sample Test						
	Test Value = 150					
	t	df	Sig. (2-tailed)	Mean Difference	95% Confidence Interval of the Difference	
					Lower	Upper
TG (mg/dl)	8.382	99	.000	36.66420	27.9851	45.3433

Table 6: LDL level in SCH

One-Sample Test						
	Test Value = 100					
	t	df	Sig. (2-tailed)	Mean Difference	95% Confidence Interval of the Difference	
					Lower	Upper
LDL (mg/dl)	15.683	99	.000	46.63260	40.7328	52.5324

Table 7: HDL level in SCH

One-Sample Test						
	Test Value = 60					
	t	df	Sig. (2-tailed)	Mean Difference	95% Confidence Interval of the Difference	
					Lower	Upper
HDL (mg/dl)	-36.914	99	.000	-30.06020	-31.6760	-28.4444

Table 8: IL-6 level in SCH

One-Sample Test						
	Test Value = 7					
	t	df	Sig. (2-tailed)	Mean Difference	95% Confidence Interval of the Difference	
					Lower	Upper
IL- (pg/ml)	19.059	99	.000	6.66740	5.9733	7.3615

Table 9: Pearson correlation between TSH and Total Cholesterol, Triglycerides, Low Density lipoprotein, High Density Lipoprotein

		TC	TG	LDL	HDL
TSH	Correlation coefficient	0.492	0.488	0.396	-0.492
	Sigma 2 tailed	<0.001	<0.001	<0.001	<0.001
	N	100	100	100	100

Table 10: Pearson correlation between TSH and Interleukin-6

	Interleukin-6(IL-6)	IL-6
TSH	Correlation coefficient	0.480
	Sigma 2 tailed	<0.001
	N	100

DISCUSSION

Hypothyroidism refers to a dysfunction in the secretion and activity of thyroid hormone. The process of ageing leads to a higher occurrence of hypothyroidism in both genders, with a larger number of women being affected compared to men. Hypothyroidism is a major public health issue, both in India and worldwide. SCH has been defined as a type of hypothyroidism condition marked by slight rise in TSH levels but normal T4 and T3 levels. The most significant outcome of SCH is an incidence of overt hypothyroidism, which is likely to manifest as a cardiovascular risk factor [5].

According to the Indian Thyroid Society the baseline of TSH in Subclinical Hypothyroidism is 4.5-10 mIU/ [1]. In our study Mean ± SD of TSH is 6.95±1.67. Hundred subjects with SCH were included, out of which 78 were female and 22 were males. The association between TSH and Interleukin-6 is statistically significant and positive, with an (r-value= 0.480) and a (p-value= 0.001). Shilpi Goyal et al. in 2022 carried out a study which found that subjects with hypothyroidism exhibited significantly increased concentrations of IL-6 and TNF-α in their blood streams in comparison to those with normal Thyroid function [10].

According to the study conducted by Taddei S et al. in 2006, individuals diagnosed with hypothyroidism showed a mild and persistent state of inflammation. This was evident of notable increase in inflammatory markers such as hs-CRP and IL-6 levels [11].IL-6 is an early inflammatory marker of inflammation and it belongs to the T-helper-2(Th2) class of cytokines, playing a crucial role in humoral immune response. Thyroid Stimulating Hormone stimulates the secretion of IL-6 from fully evolved 3T3-L1 adipocytes. This is achieved via TSH signalling through the cAMP-PKA pathway, which leads to the activation of IL-6 gene transcription [7]. Similarly, Sandeep Kumar et al, in (2023) has also found that there was elevated TSH and IL-6 in SCH patients [12].

In this study we observed significantly increased concentration of Total cholesterol, Triglycerides, and LDL in SCH subjects. The number of subjects having Total Cholesterol less than 200 mg/dl is 32 whereas 68 subjects were having more than 200mg/dl. The number of subjects having Triglycerides less than 150mg/dl is 24 whereas 76 subjects were having more than 150 mg/dl. Similarly, the number of subjects having LDL less than 100 mg/dl is 7 whereas 93 subjects were having more than 100mg/dl. The correlation between TSH and TG is statistically significant and positive, with a correlation coefficient (r-value = 0.488) and a (p-value ≤0.001). The correlation between Thyroid-Stimulating Hormone (TSH) and Total Cholesterol (TC) is statistically significant and positive, as indicated by an (r-value= 0.492) and a (p-value ≤ 0.001). The correlation between TSH and LDL is statistically significant and positive, with a correlation coefficient (r-value= 0.396) and a (p-value ≤ 0.001). The correlation between TSH and HDL is statistically significant and negative, with a correlation coefficient (r-value = -0.492) and a (p-value ≤ 0.001).

The study done by Ejaz M et al. in (2021) found that LDL-C and Total Cholesterol values were higher in patients with SCH [13]. On the other hand, comparable findings from an Indian study done by Asranna A et al. in (2012) indicated that elevated TSH levels are correlated with elevated LDL, TG, and TC levels. Hyperlipidaemia is therefore more prevalent in SCH patients [14]. Thyroid hormone has a crucial role in both the breakdown and production of lipids, exerting a major impact on lipid metabolism. Hypothyroidism can lead to a disruption in lipid metabolism, where the breakdown of lipids is more prevalent than their production [15].

In this study, we found association between dyslipidaemia and increased inflammatory markers in subject with SCH which is also supported by Gaurav G et al. in (2015) has conducted study in north India has additionally found in their study, SCH patients had higher levels of TC, TG, and LDL-C than the control group. In addition, the patients' group exhibited higher levels of inflammatory markers. IL-6, a cytokine that causes inflammation, increases the synthesis of CRP in the liver, which in turn indirectly contributes to the development of atherosclerosis [5].

CONCLUSION

İt is concluded that subjects with Subclinical Hypothyroidism (SCH) exhibit elevated levels of inflammatory markers alongside changes in their lipid profiles, increasing their susceptibility to cardiovascular disease (CVD). Thus, early diagnosis and treatment of SCH have significance in reducing the risk of cardiovascular disease. However, our study is limited by factors such as sample size and the inclusion of only one inflammatory marker. Future research should employ more robust assessment tools to better understand the cardiovascular risk associated with SCH. If left untreated, SCH may progress to overt hypothyroidism, emphasizing the need for further investigations to identify factors that could prevent this progression.

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