e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2024; 16(5); 303-307

Original Research Article

Assessment of Hs-CRP and Lipid Profile in Newly Detected Hypothyroid Adults: A Case Control Study

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Received: 04-03-2024 / Revised: 19-04-2024 / Accepted: 29-05-2024
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Conflict of interest: Nil

Abstract

Aim: The aim of the present study was to analyse the thyroid profile, hs-CRP and lipid profile in newly detected hypothyroid adults in comparison to controls and also to compare the above parameters in subclinical and clinical hypothyroid cases.

Methods: The present study was conducted in the Department of Medicine, Ford hospital and research centre Pvt. Ltd, Patna, Bihar, India. A total of 100 subjects (50 hypothyroid cases and 50 euthyroid (controls), visiting General Medicine OPD Bengaluru were consider for study.

Results: The mean age of cases and controls in our study was found to be 36.44±12.48 years and 35.95±10.25 years respectively (p = 0.65). BMI values in the study were higher in cases (26.34 ± 4.86 kg/m2) compared to controls (25.85 ± 4.52 kg/m2) and was statistically significant (P = 0.07). In the study, the mean TSH levels of cases were high compared to controls and were statistically significant. The mean serum hs -CRP levels in both the study groups was within the reference range, but it was high and statistically significant in cases than in control. The mean LDL- c value in cases and control was high in cases and the difference was statistically significant. The triglyceride levels of cases were significantly higher than that of control and were statistically significant. hs -CRP levels were in within reference range for 78% of cases and 92% controls whereas above the normal range was seen in 22% cases and only 6% controls. As per the Pearson's correlation, there was a significant positive correlation between serum TSH and hs - CRP levels in cases (r = 0.265, p < 0.001). There was a significant increase in serum TSH in CH as compared to SCH. The difference was statistically significant. hs -CRP levels though high in CH than SCH were statistically insignificant. TSH and hs- CRP when compared between SCH, CH and controls showed a statistically significant difference between groups with p value <0.001.

Conclusion: This study concluded that hypothyroidism is associated with dyslipidemia and low grade inflammation. Subclinical hypothyroidism was found to be more common than clinical hypothyroidism. Hypertriglyceridemia and at risk hs - CRP levels though seen in hypothyroid cases were more prominent in CH cases than SCH.

Keywords: hs-CRP, Thyroid stimulating hormones, Clinical hypothyroidism, Subclinical Hypothyroidism

Introduction

The World Health Organization (WHO) considers cardiovascular diseases (CVD) the most common cause of death worldwide, accounting for around 17.9 million deaths globally, more than two-thirds of which are in developing countries. CVD is a constellation of disorders involving coronary heart diseases, cerebrovascular diseases, rheumatic heart diseases, and others. Lack of physical activity, smoking, alcohol ingestion, and an unhealthy diet are important risk factors in developing CVD and are often associated with other pathological conditions like diabetes mellitus, thyroid disorders, renal dysfunction, hypertension, and dyslipidemia. [1,2] Previous studies have established a positive association between thyroid abnormality, homocysteine concentration in blood, systemic inflammatory processes, and cardiovascular diseases. [3,4]

Thyroid hormones have a vital role in maintaining the homeostasis of the cells, and its abnormalities can be classified into hypothyroidism and hyperthyroidism. Hypothyroidism can be further divided into overt hypothyroidism (OvertHO) and subclinical hypothyroidism (SCH) based on the levels of serum thyroid-stimulating hormone and serum thyroxine. [5] Hypothyroidism is characterized by low basal metabolic rate, heat generation, and oxygen expenditure. The primary mechanism by which the thyroid hormone disorder can predispose to systolic and diastolic heart failure

is by altering cardiac myocyte contractility and surface receptor-mediated remodelling of the cardiomyocyte. [6,7] There are conflicting views about hypothyroidism being an independent risk factor for developing cardiovascular pathology or mortality or as part of a group of risk factors. [8]

The National Health Nutrition Examination Survey III (NAHES III) in the United States revealed a 4.6% prevalence of hypothyroidism and a 4.3% prevalence of subclinical hypothyroidism, with a higher prevalence in women and the elderly. [5] Other studies in Europe have determined that the prevalence of undiagnosed hypothyroidism was 4.94%, with a considerable female preponderance of 8.12%. A similar trend was also observed in the Indian population, hypothyroidism was prevalent in 10.95% of Indian adults, with a higher prevalence rate in females (15.86%) than males and a higher prevalence rate in older adults (46–54 years) (13.11 %). [6,7]

The aim of the present study was to analyse the thyroid profile, hs-CRP and lipid profile in newly detected hypothyroid adults in comparison to controls and also to compare the above parameters in subclinical and clinical hypothyroid cases.

Materials and Methods

The present study was conducted in the Department of Medicine, Ford hospital and research centre Pvt. Ltd, Patna, Bihar, India for one year . A total of 100 subjects (50 hypothyroid cases and 50 euthyroid (controls), visiting General Medicine OPD Bengaluru were consider for study.

Group 1: Cases – 82 newly detected hypothyroid adults, age group: 18-55 years

Group 2: Controls – 82 normal healthy adults within same age group

Inclusion Criteria

Cases: Newly detected hypothyroid cases between age group of 18-55 years attending General medicine OPD, RRMCH, Bengaluru

Controls: Age and sex matched healthy individuals

Exclusion Criteria

1. Subjects who haven't submitted written informed consent

2. Subjects having history of any Medical/ Surgical illness like Cardio vascular disorders, Diabetes Mellitus, kidney failure, Liver disorders and other major chronic illnesses

3. Hypothyroid adults with any other medications or treatments

Method of Collection Of Data

Blood samples were collected with full aseptic precautions after obtaining informed consent. Clot activator that contains vacuum evacuated tubes for analysis of serum TSH, FT3, FT4, TC, HDL-c, LDL-c, TG, hs-CRP. Then after collection, serum samples were stored at -20º until analyzed. Anthropometric measurements for BMI, height (cm) and body weight (kg) were measured without shoes or cap.

Investigations Done

1. Serum TSH, FT3 and FT4 by CLIA

2. Serum high sensitive C reactive protein by Immuno- turbidimetric assay

3. Lipid parameters analyzed in Erba EM360 autoanalyzer, Serum TG: GPO Method, HDL and LDL cholesterol by precipitation method, Total cholesterol by cholesterol oxidase – peroxidase method.

Statistical Analysis

Analysis was done using SPSS version-20 software. The mean and standard deviation for quantitative variables were calculated for the study. Chi-square test, ANOVA test, students t test were applied whenever necessary. Pearson correlation coefficient was obtained to find out correlation between different parameters. p value < 0.05 was considered to be significant.

Results

Table 1: Comparison of cases and controls according to age and BMI

	Cases	Controls	P Value
Age	36.44±12.48	35.95±10.25	0.65
BMI (Kg/m2)	26.34 ± 4.86	25.85 ± 4.52	0.07

The mean age of cases and controls in our study was found to be 36.44±12.48 years and 35.95±10.25 years respectively (p = 0.65). BMI values in the study were higher in cases (26.34 ± 4.86 kg/m2) compared to controls (25.85 ± 4.52 kg/m2) and was statistically significant (P = 0.07).

Table 2: Comparison of cases ad controls with biochemical parameters

	Hypothyroid Cases n=50	Controls n=50	P value
T H µIU/ml	14.28 ± 8.8	2.4 ± 0.94	<0.001
FT3 pg/ml	1.8 ± 0.8	2.2± 0.8	0.48
FT4 ng/ml	0.8 ± 0.4	0.8 ± 0.09	1.00
hs-CRP mg/l	4.0 ± 2.8	2.8 ± 2.6	0.007
Total Cholesterol (mg/dl)	182.78 ± 40.48	184.24±26.14	0.72
HDL-c (mg/dl)	46.20±8.97	53.0±6.3	< .001
LDL-c(mg/dl)	145.52±32.98	132.68±32.42	0.01
TG (mg/dl)	158.90±51.64	145.65±28.35	0.05

In the study, the mean TSH levels of cases were high compared to controls and were statistically significant. The mean serum hs -CRP levels in both the study groups was within the reference range, but it was high and statistically significant in cases than in control. The total cholesterol level in cases and control were within the reference range and there was no statistical significance. Further it was found that HDL-c in cases and control were found to be lower in cases compared to controls and the difference was statistically significant. The mean LDL- c value in cases and control was high in cases and the difference was statistically significant. The triglyceride levels of cases were significantly higher than that of control and were statistically significant.

Table 3: Distribution of cases and controls according to their hs-CRP and Pearson's correlation coefficient between T H vs hs-CRP

		Hypothyroid Cases =50 39 (78%)	Controls n=50 46 (92%)
hs-CRP mg/l	< 5 mg/l		
≥ 5 mg/l		11 (22%)	4 (8%)
Chi square value =7.043, p value = 0.007			
Parameters	**r value**	**P value**	
T H vs hs-CRP	0.265	<0.001	

hs -CRP levels were in within reference range for 78% of cases and 92% controls whereas above the normal range was seen in 22% cases and only 6% controls. As per the Pearson's correlation, there was a significant positive correlation between serum TSH and hs - CRP levels in cases ($r = 0.265$, $p < 0.001$).

Table 4: Comparison of various parameters among CH and SCH

Parameter	CH =15	SCH n=35	p value
Age (years)	37.72 ± 12.02	34.17 ±11.07	.16
BMI (kgm2)	26.36 ± 3.97	26.30 ± 5.35	.12
TSH (µIU/ml)	23.7 ± 8.7	9.0 ± 2.4	< .001
FT3 (pg/ml)	1.2 ± 0.7	2.3 ± 0.4	< .001
FT4 (ng/ml)	0.5 ± .3	1.0 ± 0.2	< .001
hs-CRP (mg/l)	4.2 ± 3.5	3.9 ± 2.3	.60
TC (mg/dl)	175.9 ± 31.1	188.8 ± 44.9	.15
HDL-C (mg/dl)	45.5 ± 9.4	46.5 ± 8.7	.61
LDL-C (mg/dl)	148.4 ± 37.0	142.3 ± 32.3	.43
TG (mg/dl)	208.2 ± 21.6	156.8 ± 52.9	< .001

There was a significant increase in serum TSH in CH as compared to SCH. The difference was statistically significant. hs -CRP levels though high in CH than SCH were statistically insignificant. Total cholesterol value was within the reference range in both the groups (CH and SCH) whereas TG was found to be high in CH compared to SCH and was found to be significant. There was no significant difference in HDL-c and LDL-c between the two groups (SCH & CH).

Table 5: ANOVA of various parameters of SCH, CH and controls

Variables	CH (n=35)	CH (n=15)	Controls (=50)	Total	F value	P value
T H	9.09±2.46	23.70±8.74	1.88± 0.96	8.07±8.86	326.52	< .001
hs- CRP	3.96±2.35	4.23±3.56	2.07±2.6	3.06±2.92	10.63	< .001

TSH and hs- CRP when compared between SCH, CH and controls showed a statistically significant difference between groups with p value <0.001.

Discussion

Thyroid dysfunction is one of the most prevalent endocrinopathies across the globe. [9] The prevalence of spontaneous hypothyroidism is 1-2% of all the thyroid disorders in the world. [10] In India thyroid disorders are the second most common glandular disorder of the endocrine system and are increasing predominantly among women. [11] Hypothyroidism is characterized by deficient thyroid hormone production which can be severe or moderate. [12] Common etiologies of hypothyroidism are dietary deficiency of iodine and Hashimotos thyroiditis, an auto-immune disease.[13]

The mean age of cases and controls in our study was found to be 36.44±12.48 years and 35.95±10.25 years respectively (p = 0.65). BMI values in the study were higher in cases (26.34 ± 4.86 kg/m2) compared to controls (25.85 ± 4.52 kg/m2) and was statistically significant (P = 0.07). Devika Tayal et al (2012) in their study observed a similar female predominance with a female to male ratio of 2.86 (females 5542 vs Males 1933) A redox imbalance elicited by estrogen could be responsible for increased prevalence in female. [14,15] In the study, the mean TSH levels of cases were high compared to controls and were statistically significant. The mean serum hs -CRP levels in both the study groups was within the reference range, but it was high and statistically significant in cases than in control. The total cholesterol level in cases and control were within the reference range and there was no statistical significance. Further it was found that HDL-c in cases and control were found to be lower in cases compared to controls and the difference was statistically significant. The mean LDL- c value in cases and control was high in cases and the difference was statistically significant. Study done by Mohsin Shafi et al [16] (2013) on newly detected hypothyroid patients found that mean TSH levels higher in cases as compared to control (14.3 ± 10.1 μIU/L vs 1.8 ±0.7) and was statistically significant (p<0.01).

The triglyceride levels of cases were significantly higher than that of control and were statistically significant. hs -CRP levels were in within reference range for 78% of cases and 92% controls whereas above the normal range was seen in 22% cases and only 6% controls. As per the Pearson's correlation, there was a significant positive correlation between serum TSH and hs - CRP levels in cases (r = 0.265, p < 0.001). Christcrain et al [17] (2003) observed an elevation in CRP levels with progressive thyroid failure and a clear association between hypothyroidism and increased hs- CRP. Thyroid disorders are known to influence lipid metabolism and other CV risk factors predominantly. Dyslipidaemia is a well-recognized association of thyroid dysfunction which should be considered in the process of evaluating and treating dyslipidemic patients. [18,19]

There was a significant increase in serum TSH in CH as compared to SCH. The difference was statistically significant. hs -CRP levels though high in CH than SCH were statistically insignificant. Total cholesterol value was within the reference range in both the groups (CH and SCH) whereas TG was found to be high in CH compared to SCH and was found to be significant. There was no significant difference in HDL-c and LDL-c between the two groups (SCH & CH). TSH and hs- CRP when compared between SCH, CH and controls showed a statistically significant difference between groups with p value <0.001. In clinical hypothyroidism (CH), a decrease in LPL activity and the clearance of TG-rich lipoproteins are found. [20] Therefore CH patients may also present with elevated TG levels associated with increased levels of VLDL and occasionally fasting chylomicronemia as observed with hypertriglyceridemia in hypothyroid cases in the study. [21] Many previous studies concluded that CH patients have elevated atherogenic and oxidative stress markers. Hence, serum TSH measurement is the essential test for diagnosis of mild thyroid failure when the peripheral thyroid hormone levels are within normal reference range. [22]

In this study, a decreased HDL levels in cases was found. Clinical studies however reported a conflicting result about HDL-cholesterol plasma levels in hypothyroidism. The studies conducted by Caron et al found a reduction in HDL cholesterol and an increase in HDL after subsequent treatment with thyroxine. However, S. Valdemarssonet et al and E. Muls et al found an improvement in the mean HDL levels in the hypothyroidism with a reduction after treatment. Several proteins related with HDL metabolism are affected by thyroid hormones. [23-25]

Conclusion

This study concluded that hypothyroidism is associated with dyslipidemia and low grade inflammation. Subclinical hypothyroidism was found to be more common than clinical hypothyroidism. Hypertriglyceridemia and at risk hs - CRP levels though seen in hypothyroid cases were more prominent in CH cases than SCH. The mild and inconsistent changes which were observed in the biochemical parameters in hypothyroidism (i.e. combination of both CH and SCH) may be due to the preponderance of subclinical hypothyroid cases in this study. However, dyslipidemia and inflammatory markers were found to be increased in

the cases that helped in prediction and evaluation of patients at risk of cardiovascular disease.

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