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Original Research Article

Hospital Based Case Control Study of Hs-CRP and Lipid Profile in Hypothyroid Adults at Bihar Region

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Abstract

Aim: 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.

Material & Methods: This was a hospital-based case control study conducted at the Department of Cardiology, IGIMS, Patna, Bihar, India for 1 year.

Results: BMI values in the study were higher in cases (25.48 ± 5.82 kg/m2) compared to controls (25.21 ± 5,62 kg/m2) and was statistically significant (P = 0.05). hs -CRP levels were in within reference range for 80% of cases and 92% controls whereas above the normal range was seen in 20 % cases and only 8 % controls.

Conclusion: Hypothyroidism (CH & SCH) is common among females and is associated with mild dyslipidemia and low-grade inflammation. Moreover, subclinical hypothyroidism is more common than clinical hypothyroidism.

Keywords: hs-CRP, lipid profile, hypothyroid

Introduction

The thyroid gland maintains the level of metabolism in the tissues that is optimal for their normal function. The principal hormones secreted by the thyroid are thyroxine (T4) and triiodothyronine (T3). The human thyroid secretes about 80µg of T4, 4µg of T3 and 2µg of RT3 per day. [1] Subclinical hypothyroidism is defined as an elevated serum TSH level associated with normal total or free T4 and T3 values. The overall prevalence has been reported to range from 6 – 8% in women and 3% in men. Because of the frequency with which this condition is encountered, important questions have been raised regarding its clinical relevance and appropriate management. Worldwide, too little iodine in the diet is the most common cause of hypothyroidism. Hashimoto's thyroiditis is the most common cause of hypothyroidism in countries with sufficient dietary iodine. Less common causes include previous treatment with radioactive iodine, injury to the hypothalamus or the anterior pituitary gland, certain medications, a lack of a functioning thyroid at birth, or previous thyroid surgery. The diagnosis of hypothyroidism, when suspected, can be confirmed with blood tests measuring thyroid-stimulating hormone (TSH) and thyroxine levels. [2]

Worldwide about one billion people are estimated to be iodine-deficient; however,

it is unknown how often this results in hypothyroidism. In the United States, hypothyroidism occurs in 0.3–0.4% of people. Subclinical hypothyroidism, a milder form of hypothyroidism characterized by normal thyroxine levels and an elevated TSH level, is thought to occur in 4.3–8.5% of people in the United States. Hypothyroidism is more common in women than in men.[3] Hypothyroidism is one of the main causes of abnormal lipid metabolism. [4,5] Patients with overt hypothyroidism are at risk of hypertension, cardiovascular disease, and atherosclerosis.[6] Lipid abnormalities in overt hypothyroidism includes elevated total cholesterol (TC), low density lipoprotein cholesterol (LDL-C) and triglycerides (TG). [5] Although the association between subclinical hypothyroidism (SCH) and dyslipidemia is still controversial, changes in lipid profile in these patients have been observed in several studies. [7]

High sensitive c- reactive protein (hs -CRP) is a marker of chronic subclinical inflammation. Increased hs -CRP levels might be a key molecule linking inflammation to oxidative stress in atherosclerosis (Singh et al) leading to CV risk.

[8] Possible role of CRP in atherogenesis might be due to enhanced expression of local endothelial cell surface adhesion molecules, endothelin 1, reduced endothelial nitric oxide bioactivity. To explore the moderate elevations as in screening, performance of hs-CRP is recommended to better identify CRP variations. [9-10]

Circulating concentrations of CRP fluctuate widely during acute responses to tissue damage or infection. It is a potential marker of more subtle and persistent systemic alterations that may be known as low grade inflammation.

[11] Possible role of CRP in atherogenesis might be due to enhanced expression of local endothelial cell surface adhesion molecules, endothelin 1, reduced endothelial nitric oxide bioactivity. To explore the moderate elevations as in screening, performance of hs-CRP is recommended to better identify CRP variations. [12-13]

In our study we hypothesized that hypothyroidism is associated with mild dyslipidemia associated with chronic inflammatory state as measured by hs-CRP. The basic aim is to study the same in the newly detected hypothyroid adults

Material & Methods:

This was a hospital based case control study was conducted at the Department of Cardiology, IGIMS, Patna, Bihar, India for 1 year

Inclusion criteria:

Cases: Newly detected hypothyroid cases between age group of 18-55 years.

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.

Groups

Group 1: Cases – 100 newly detected hypothyroid adults, age group: 18-55 years

Group 2: Controls – 100 normal healthy adults within same age group

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 Immunoturbidimetric 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.

Results:

As shown in Table 1, both cases and controls were age matched. The mean age of cases and controls in our study was found to be 34.71 ±11.77 years and 34.31±10.82 years respectively (p = 0.81). Approximately 92% of cases and 75% of controls were females depicting a female preponderance (Figure 1). BMI values in the study were higher in cases (25.48 ± 5.82 kg/m2) compared to controls (25.21 ± 5,62 kg/m2) and was statistically significant (P = 0.05) (Table 1)

In the study, the mean TSH levels (14.61 ± 8.0 µIU/ml) of cases were high compared to controls and was statistically significant (p <0.001) (Table 2). The mean serum hs -CRP levels in both the study groups were within the reference range, but it was high and statistically significant in cases than in control (p = 0.005). The total cholesterol level in cases (180.4 ± 40.7 mg/dl) and control (183.71 ± 27.61 mg/dl) were within the reference range and there was no statistical significance (p = 0.90). Further it was found that HDL-c in cases (46.22±8.71 mg/dl) and control (51.3 ± 6.9 mg/dl) were found to be lower in cases compared to controls and the difference was statistically significant (p <0.001). The mean LDLc value in cases (145.7±33.71 mg/dl) and control (129.8 ± 30.3 mg/dl) was high in cases and the difference was statistically significant (p = 0.01). The triglyceride levels of cases (157.8±50.3 mg/dl) were significantly higher than that of control (142.7 ± 27.8 mg/dl) and was statistically significant (p = 0.05).

As in Table 3, hs -CRP levels were in within reference range for 80% of cases and 92% controls whereas above the normal range was seen in 20 % cases and only 8 % controls.

As per the Pearson's correlation, there was a significant positive correlation between serum TSH and hs CRP levels in cases (r = 0.331, p <0.001). (Table 4)

In Table 5, the mean age, BMI between the two groups did not differ significantly. There was a significant increase in serum TSH in CH (24.8 ± 8.6 µIU/ml) as compared to SCH (9.0 ± 2.4 µIU/ml). The difference was statistically significant (p <0.001). hs -CRP levels though high in CH than SCH were statistically insignificant (p = 0.78). 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 (p < 0.001). There was no significant difference in HDL-c and LDL-c between the two groups (SCH & CH).

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

	Cases n=100	Controls n=100
Age BMI (Kg/m2)	34.71±11.77 25.48± 5.82	34.31±10.82 25.21± 5,62

Table 2: Comparison of cases ad controls with biochemical parameters

	Hypothyroid Cases n=100	Controls n=100
T H µIU/ml	14.61± 8.0	2.4 ± 0.88
FT3 pg/ml	1.6± 0.8	2.5 ± 0.8
FT4ng/ml hs-	0.8 ± 0.5	0.8 ± 0.09
CRP mg/l	4.2± 2.6	2.8± 2.5
Total Cholesterol (mg/dl)	180.4± 40.7	183.71 ±27.61
HDL-c (mg/dl)	46.22±8.71	51.3 ±6.9
LDL-c(mg/dl)	145.7±33.71	129.8 ±30.3
TG (mg/dl)	157.8±50.3	142.7 ±27.8

Table 3: Distribution of cases and controls according to their hs-CRP

		Hypothyroid Cases = 100	Controls n= 100
hs-CRP mg/l	<5 mg/l	80	92
	≥ 5 mg/l	20	8
	Total	100	100

Table 4: Pearson's correlation coefficient between T H vs h s-CRP

Parameters	r value	P value
T H vs hs-CRP	0.331**	<0.001

Table 5: Comparison of various parameters among CH and SCH

Parameter	CH = 31	SCH n= 65
Age (years)	35.71± 12.72	33.2± 11.3
BMI (kgm2)	26.33± 3.81	25.8± 5.77
TSH (µIU/ml)	24.8± 8.6	9.0 ± 2.4
FT3 (pg/ml)	1.3± 0.8	2.3 ± 0.5
FT4 (ng/ml)	0.6± 0.3	1.5± 0.6
hs-CRP (mg/l)	4.6± 3.8	3.0± 2.6
TC (mg/dl)	173.6± 30.6	187.8± 45.8
HDL-C (mg/dl)	45.7± 9.5	44.6± 8.6
LDL-C (mg/dl)	143.8± 36.4	140.6± 31.3
TG (mg/dl)	202.8± 20.2	155.4± 52.8

Discussion:

Using data from the NHANES in the United States, a cross-sectional analysis of 1,551 euthyroid subjects and 57 with SCH did not find any association between ln(hs-CRP) and SCH (β = –0.017, p = 0.941). The sample in this study had a slight predominance of men (51%) and whites

(52%), and was older (≥40 years of age). Multivariate linear adjustment was done for age, gender, race, use of cholesterol-lowering medication, and a composite of diabetes and prevalence of cardiovascular disease, hypertension, smoking, and obesity [14].

Similar to the NHANES data, other studies with different designs were not able to show a consistent association between SCH and increased hs-CRP. One Swiss double-blind placebo-controlled clinical trial showed that hs-CRP values increased progressively with thyroid failure in 63 subjects with SCH ($p = 0.022$), and particularly in 61 subjects with overt hypothyroidism ($p = 0.016$), in comparison to 40 euthyroid matched controls. However, levothyroxine therapy over 48 weeks did not result in decreased hs-CRP in 31 subjects with SCH compared to 32 subjects with SCH randomized to the placebo group [15]. Consistent with this clinical trial, one retrospective South Korean study that followed individuals with SCH who were treated or not with levothyroxine did not find decreased serum hs-CRP levels in either group [16].

Hypothyroidism is a disorder presenting with different degrees of thyroid failure and metabolic consequences. An increase of serum TSH is a very early biochemical marker of impending thyroid failure resulting from the gradual decline of T4 and at a later stage of T3. SCH is a frequent syndrome and has been defined as a condition with normal circulating levels of T3 and T4 but elevated TSH. Lipid levels and hs-CRP are known cardiovascular risk factors and the following study focuses on these two risk factors and their possible link with SCH. The thyroid gland maintains the level of metabolism in the tissues that is optimal for their normal function. The principal hormones secreted by the thyroid are thyroxine (T4) and triiodothyronine (T3). The human thyroid secretes about 80µg of T4, 4µg of T3 and 2µg of RT3 per day. [17] Subclinical hypothyroidism is defined as an elevated serum TSH level associated with normal total or free T4 and T3 values. The overall prevalence has been reported to range from 6–8% in women and 3% in men. Because of the frequency with which this condition is encountered, important questions have been raised regarding its clinical relevance and appropriate management. [18]

Sunanda et al (2012) found that there was a strong positive association between TSH and lipid profile in hypothyroid patients and concluded that effect of hypothyroidism on the serum lipids is more pertinent in patients with higher TSH levels.[19] Khan Mah et al(2013) also found a significant dyslipedemia i.e. significant increase in TC, LDL-c and TG levels and decrease in HDL-c levels. [20]

For better analysis in this study, hypothyroid cases were divided into subclinical hypothyroid (SCH) and clinical hypothyroid (CH). Majority of the target study group was female. The mean age, BMI values between two groups did not differ significantly. The CH subjects has higher serum TSH levels as compared to the subjects of SCH which was statistically significant ($P<0.001$). hs -CRP levels were found to be at risk level and was comparable in both CH and SCH but was statistically insignificant ($p=0.64$). Many studies have shown that high levels hsCRP in women with SCH correlated with parameters of obesity which emphasizes the role of body weight in inflammation [21] and may consider as an additional risk factor for the development of atherosclerosis and CVD.[22-24]

Conclusion:

Hypothyroidism (CH & SCH) is frequent among females and is related with modest dyslipidemia and low-grade inflammation. Moreover, subclinical hypothyroidism is more prevalent than clinical

hypothyroidism. The moderate and inconsistent alterations which were seen in the biochemical markers in hypothyroidism (i.e. combination of both CH and SCH) may be attributable to the majority of subclinical hypothyroid individuals in our investigation. However, dyslipidemia and inflammatory markers were found to be raised in the instances that aided in prediction and assessment of individuals at risk of cardiovascular disease

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