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Original Research Article

Evaluation of Thyroid Profile, High-Sensitivity C-Reactive Protein (Hs-Crp), and Lipid Profile Alterations in Newly Diagnosed Hypothyroid Adult Patients: A Case-Control Study

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Abstract:

Background: To analyse the thyroid profile, hs-CRP and lipid profile in newly detected hypothyroid adults in comparison to controlsand also to compare the above parameters in subclinical and clinical hypothyroid cases.

Material and Methods: The study was a cross sectional study which was carried JNKTMCH, Madhepura Study duration is Two years. Total 240 patients were divided into 2 groups. Group-1 for newly detected hypothyroid adults and Group 2 as Controls. 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 -20^0 until analyzed. Anthropometric measurements for BMI, height (cm) and body weight (kg) were measured.

Results: The mean age of cases and controls in our study was found to be 36.12±12.21years and 35.87±11.06years respectively (p = 0.81). BMI values in the study were higher in cases (27.24 ± 4.65kg/m2) compared to controls (25.17 ± 4.37kg/m2) and was statistically significant (P = 0.03). In the study, the mean TSH levels (15.27 ± 9.2µIU/ml) of cases were high compared to controls (3.1 ± 0.88µIU/ml) and were statistically significant (p<0.001). 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 (p = 0.004). The total cholesterol level in cases (182.29 ± 39.75mg/dl) and control (184.27±28.37mg/dl) were within the referencerange and there was no statistical significance (p = 0.82).

Conclusion: we concluded that the hypertriglyceridemia and at risk hs-CRP levels though seen in hypothyroid cases were more prominent in CH cases than SCH. 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.

Keywords: CRP, TSH, HDL, LDL.

Introduction

Hypothyroidism is a common endocrine disorder resulting from deficiency of thyroid hormone. In the United States and other areas of adequate iodine intake, autoimmune thyroid disease (Hashimoto disease) is the most common cause of hypothyroidism; worldwide, iodine deficiency remains the foremost cause. Hypothyroidism, also called underactive thyroid or low thyroid, is a disorder of the endocrine system in which the thyroid gland does not produce enough thyroid hormone. It can cause a number of symptoms, such as poor ability to tolerate cold, a feeling of tiredness, constipation, depression, and weight gain. Occasionally there may be swelling of the front part of the neck due to goiter. Untreated cases of hypothyroidism during pregnancy can lead to delays in growth and intellectual development in the baby or congenital iodine deficiency syndrome. [1] 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 aboutone 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 lipidmetabolism. [4,5] Patients with overt hypothyroidism are at risk of hypertension, cardiovascular disease, and atherosclerosis. [6] Lipid abnormalities in overthypothyroidism 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 toenhanced 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] 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 and Methods

The study was a cross sectional study which was carried in JNKTMCH, Madhepura. Study duration is Two years. Total 240 patients weredivided into 2 groups. in Group-1: 120 newly detected hypothyroid adults and Group 2: Controls – 120 normal healthy adults within same age group. Institutional ethical committee clearance was obtained.

Inclusion Criteria

- Newly detected hypothyroid cases

Exclusion Criteria

- Cardio vascular disorders,
- Diabetes Mellitus,
- kidney failure,
- Liver disorders
- Cerebrovascular accidents
- Obesity
- Infections
- Drugs

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. Serum TSH, FT3 and FT4 by CLIA, Serum high sensitive C reactive protein by Immunoturbidimetric assay and Lipid parameters analyzed in Erba EM360 autoanalyzer, Serum TG: GPO Method, HDL and LDL cholesterol by precipitation method, Total cholesterol by cholesteroloxidase – peroxidase method were investigated .

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 36.12±12.21years and 35.87±11.06years respectively ($p = 0.81$). Approximately 90% of cases and 80% of controls were females depicting a female preponderance BMI values in the study were higher in cases (27.24 ± 4.65kg/m2) compared to controls (25.17 ± 4.37kg/m2) and was statistically significant ($P = 0.03$) (Table 1) In the study, the mean TSH levels (15.27 ± 9.2µIU/ml) of cases were high compared to controls (3.1 ± 0.88µIU/ml) and was statistically significant ($p < 0.001$) (Table 2).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 ($p = 0.004$). The total cholesterol level in cases (182.29 ± 39.75mg/dl) and control (184.27±28.37mg/dl) were within the reference range and there was no statistical significance ($p = 0.82$). Further it was found that HDL-c in cases (45.89±9.47mg/dl) and control (52.87±6.7mg/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 (145.14±34.12mg/dl) and control (132.05±32.14mg/dl) was high in cases and the difference was statistically significant ($p = 0.01$). The triglyceride levels of cases (159.26±49.87mg/dl) were significantly higher than that of control (146.23±29.27mg/dl) and was statistically significant ($p = 0.03$). As in Table 3, hs -CRP levels were in within reference range for 92 (76.67%) of cases and 109(90.83%) controls whereas above the normal range was seen in 28 (23.33%) cases and only 11(9.17%) controls. (Table 4)As per the Pearson's correlation, there was a significant positive correlation between serum TSH and hs -CRP levels in cases ($r = 0.24$, $p < 0.001$).

To analyse the condition, Hypothyroid cases (n = 120) in our study was divided into two groups (subclinical hypothyroid and clinical hypothyroid) based on TSH and thyroid hormone levels. Out of 120, 64.17% (n = 77) were subclinical hypothyroid (SCH) and 35.83% (n=43) wereclinical hypothyroid (CH) cases. A definite female preponderance was observed in the study. 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 (24.11 ± 9.1µIU/ml) as compared to SCH (10.2 ± 2.2 µIU/ml). The difference was statistically

significant($p < 0.001$). hs-CRP levels though high in CH than SCH were statistically insignificant ($p = 0.58$). 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). TSH and hs- CRP when compared between SCH, CH and controls showed a statistically significant difference between groupswith p value<0.001. (Table 6)

Table 1: Comparison with age and BMI

	Cases n=120	Controls n=120	P Value
Age	36.12±12.21	35.87±11.06	0.81
BMI (Kg/m2)	27.24 ± 4.65	25.17 ± 4.37	= 0.03*

Table 2: Comparison of biochemical parameters

Parameter	Case 120	Control =120	P value
T H µIU/ml	15.27 ± 9.2	3.1 ± 0.88	<0.001*
FT3 pg/ml	1.8 ± 0.7	2.0± 0.8	= 0.38
FT4 ng/ml	0.8 ± 0.5	0.8 ± 0.08	= 1.00
hs-CRP mg/l	4.1 ± 2.7	2.9 ± 2.4	= 0.004*
Total Cholesterol (mg/dl)	182.29 ± 39.75	184.27±28.37	= 0.82
HDL-c (mg/dl)	45.89±9.47	52.87±6.7	< .001*
LDL-c(mg/dl)	145.14±34.12	132.05±32.14	= 0.01*
TG (mg/dl)	159.26±49.87	146.23±29.27	= 0.03*

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

hs-CRP mg/l < 5 mg/l	Hypothyroid Cases =120 92 (76.67%)	Controls n=120 109(90.83%)
≥ 5 mg/l	28 (23.33%)	11(9.17%)
Chi square value =7.029, p value = 0.008		

Table 4: Pearson's correlation coefficient between TSH vs hs-CRP

Parameters	r value	P value
TSH vs hs-CRP	0.242**	<0.001

Table 5: Comparison of various parameters among CH and SCH

Parameter	CH =43	SCH n=77	p value
Age (years)	38.12 ± 12.11	35.18 ±11.24	= .14
BMI (kgm2)	26.45± 4.36	26.39 ± 5.24	= .14
TSH (µIU/ml)	24.11 ± 9.1	10.2 ± 2.2	< .001*
FT3 (pg/ml)	1.4 ± 0.9	2.5 ± 0.5	< .001*
FT4 (ng/ml)	0.6 ± .4	1.1 ± 0.3	< .001*
hs-CRP (mg/l)	4.4± 3.7	4.1 ± 2.5	= .58
TC (mg/dl)	176.4± 32.6	189.7 ± 45.7	= .17
HDL-C (mg/dl)	45.7 ± 8.9	46.2 ± 8.5	= .58
LDL-C (mg/dl)	151.24 ± 36.8	142.8 ± 33.2	= .36
TG (mg/dl)	107.54 ± 20.4	158.23 ± 51.4	< .001*

Table 6: Anova of various parameters of SCH, CH and control

Variables	SCH (n=77)	CH (n=43)	Controls	Total	F value	P value
T H	10.2 ± 2.2	24.11 ± 9.1	1.92± 0.89	8.37±8.75	317.47	< .001
hs- CRP	3.96±2.35	4.23±3.56	2.07±2.6	3.06±2.92	10.63	< .001

Discussion

Hypothyroidism is by far the most prevalent form of thyroid disorder and is more common in women. [11] It is characterized by a broad clinical spectrum ranging from an asymptomatic/subclinical condition to over the state of myxoedema, end organ effects and multi organ failure. [12] This study has investigated the possible association of hypothyroidism with hs-CRP, lipid profile both reportedly associated with risk of CVD. A total of 240 subjects participated in this study. Out of the total 120 subjects were newly detected hypothyroid subjects (cases) and 120 were healthy control. Both the cases and control were age matched. The mean age of cases and control was 36.12±12.21years and

35.87±11.06 years respectively (p=0.81). Thyroid dysfunction is a common endocrine disorder with its prevalence increasing with age. About90% of cases and 80% of control were females showing a female preponderance. Hypothyroidism is known to inflict females more than males. Devika Tayal et al 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. [13,14] In this study BMI was higher in hypothyroid cases. Study conducted by Nivedita Nanda et al., Kunal B.K. [15] et al reported similar observation with BMI in hypothyroidism. Thyroid hormones mediate their effects mainly through mechanism that stimulate basal metabolic rate, increase ATP expenditure, modulate adrenergic receptor number and responsiveness to catecholamines. Hypothyroid state characterized by slowing down of basal metabolic rate may be an important factor contributing to increase BMI in these cases. Themean level of serum TSH was significantly higher in cases compared to control (15.27 ± 9.2vs 3.1 ± 0.88µIU/mL)respectively and was statistically significant (p< 0.001).The mean serum FT3 levels (1.8 ± 0.7 vs 2.0 ± 0.8 pg/ml, p = 0.38) and serum FT4 levels (0.8 ± 0.5 vs 0.8 ± 0.08 ng/ml, p = 1.0) in both cases and control respectively were within the normal range (Table 2). Study done by Mohsin Shafi et al on newly detected hypothyroid patients found that mean TSH levels higher in cases as compared to control (15.27 ± 9.2µIU/L vs 3.1 ± 0.88) and was statistically significant (p < 0.01). [16] Thyroid. hormone plays a crucial role in regulation of immune system and has the potential to dampen inflammatory cytokines such as INF-α, IL-6, IL-10. Several signs and symptoms suggest that hypothyroidism is an inflammatory state resulting frominteraction of IL-6 on TNF and IL-1 leading to increase hs -CRP in this state. Recent studies found that moderate elevations of CRP correlate with future cardiovascular events justifying the use of this test to evaluate cardiovascular risk. [17] This study showed that mean serum hs -CRP levels in both study groups were within reference range but the mean serum hs-CRP levels in cases was significantly higher (p=0.005) than in control. A significant positive correlation was also found between serum TSH and hs-CRP levels in cases (r = 0.242, p < 0.001). Christ- crain et al (200 3) observed an elevation in CRP levels withprogressive thyroid failure and a clear association between hypothyroidism and increased hsCRP. [18] Tuzcu et al , Alpaslan T et al [17] in their studies of the association between coronary heart disease and SCH have reported thatelevated hs -CRP levels suggest low grade inflammation predictive of CV risk in hypothyroid subjects. [17] In contrary to this, a study conducted by Aksoy DY et al on women could not validate a significant difference in hs-CRP levels between hypothyroid and control. [19] The interaction of IL-6 on TNF-α and IL-1 results in the raised CRP levels inhypothyroidism. Lack of thyroid hormones may impair the rate of CRP clearance which may be one reason in increase in serum CRP level. Similarly, slow CRP uptake in target cells might also add to this phenomenon. The low grade inflammation which may be accountable for increased risk of developing CVD in hypothyroidism. [20] Thyroid disordersare 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. [21,22]

Conclusion

We concluded that the hypertriglyceridemia and at risk hs- CRP levels though seen in hypothyroid cases were more prominent in CH cases than SCH. 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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