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# CORRELATION OF HIGH SENSITIVTY C-REACTIVE PROTEIN (hs-CRP) AND BODY MASS INDEX (BMI) IN SUBCLINICAL HYPOTHYROIDISM

**Kasak Chaudhary [1], S. B. Sharma [2], Thuraya Abdulsalam A. A. Al- Azazi [3], Manoj Kumar Nandkeoliar [4], Bhumesh Tyagi [5], Vikram Singh Chauhan [6] and Aisha Beg [7]***

[1] M.Sc Student Third Year, Department of Biochemistry, School of Medical Science & Research, Sharda University.
[2,4] Professor, Department of Biochemistry, School of Medical Science & Research, Sharda University.
[3] PhD Scholar, Department of Biochemistry, School of Medical Science & Research, Sharda University.
[5] Assistant Professor, Department of Medicine, School of Medical Science & Research, Sharda University.
[6] Professor, Department of Surgery, School of Medical Science & Research, Sharda University.
[7] Assistant Professor, Department of Biochemistry, School of Medical Science & Research, Sharda University.
*Corresponding Author Email: aisha.beg@sharda.ac.in

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**Abstract**

**Background:** Thyroid disease is a prevalent endocrine disorder worldwide. Subclinical or mild hypothyroidism commonly known as early thyroid failure, is characterized by normal total or free thyroxine and triiodothyronine concentrations along with high thyroid stimulating hormone level. Hypothyroidism and obesity are two prevalent clinical illnesses with a close connection. High Sensitivity C-reactive Protein is an indicator of future cardiovascular events and directly contributes to the pathophysiology of atherosclerosis. This study was carried out in North Indian population to ascertain the link between high sensitivity c-reactive protein and body mass index in subclinical hypothyroidism. **Aim and Objectives:** To study the correlation of High Sensitivity C-Reactive Protein (hs-CRP) and Body Mass Index (BMI) in Subclinical Hypothyroidism (SCH). **Materials and methods:** A cross sectional study 100 subclinical hypothyroidism subjects in the age group 18 to 60 years were included. BMI measured by Welcare Accuniq BC310. Serum TSH, Total T3, Total T4 and Serum hs-CRP levels were measured by ELISA. **Result:** Serum TSH is significantly correlated with Serum hs-CRP (r=0.4554, p= 0.001) and BMI (r= 0.3413, p= 0.002) whereas hs-CRP is non-significantly correlated with BMI (r= 0.2129, p= 0.061). **Conclusion:** It is concluded that in patients with subclinical hypothyroidism, there is a significant association between hs-CRP and BMI with TSH. Early recognition of SCH may help to prevent the progression to overt hypothyroidism. Elevated TSH levels are associated with both obesity and overweight. Regular physical activity, balanced diet, and healthy lifestyle, performing regular yoga may protect overall health and in prevention of obesity and its associated health complications.

**Keywords:** SCH, TSH, T4, T3, hs-CRP, BMI.

## INTRODUCTION

Subclinical or Mild Hypothyroidism, commonly known as early thyroid failure, it affects more women than males [1]. Subclinical hypothyroidism (SCH) is characterized by normal total or free T4 and T3 concentrations along with high TSH level [2]. According to the Indian Thyroid Society, the baseline of TSH in SCH is 4.5 to 10 mIU/L [3]. Each year, around 2-5% of SCH cases progress to overt hypothyroidism [4].

Thyroid gland dysfunction is a common endocrine disorder in India. The study found that subclinical hypothyroidism (SCH) had a frequency of 9.4% and hypothyroidism

had a prevalence of 3.9%. Women were more likely to have both conditions, with 11.4% of women affected compared to 6.2% of men [5].

The liver produces an acute-phase protein called hs-CRP in reaction to long-term inflammatory conditions and infections. hs-CRP is a predictor of future cardiovascular events and most likely directly contributes to the pathogenesis of atherosclerosis through alterations in coronary artery smooth muscle cells and endothelial cells [6].

Increased monocyte migration into atheromatous plaque brought on by hs-CRP ultimately results in endothelial dysfunction by triggering nitric oxide production from vascular endothelium. When systemic vascular endothelial cells and coronary artery endothelial cells are exposed to hs-CRP, they exhibit increased plasminogen activator inhibitor-1 and other adhesion molecules [7].

BMI is determined by dividing body mass by the square of body height, measured in kilograms per meter squared ($kg/m^2$) [8]. A person's BMI can be used to categorize them as Underweight, Normal weight, Overweight, Obese, or Severe Obese based on their tissue mass and height [9].

Hypothyroidism and obesity are two prevalent clinical disorders that have a close connection. Patients usually consider obesity as an indirect consequence of thyroid disease.

Clinical research indicates that SCH, A modest form of thyroid dysfunction is related with considerable changes in body weight and may potentially be a risk factor for obesity and overweight [10].

## MATERIALS AND METHODS

The study was carried out in the Department of Biochemistry & Central Research Laboratory & Department of Medicine, School of Medical Sciences and Research (SMS&R), Sharda University, Greater Noida, India, after obtaining ethical clearance. This is a cross-sectional study including 100 individuals with SCH.

Subjects with Subclinical hypothyroidism (having TSH level from 4.5-10 mIU/L with normal T3, T4 level) in age group between 18-60 years were included in study. Known cases of other endocrine disorders, Pregnancy, Women on contraceptive pills,and Patients on medication were excluded.

### Anthropometric Measurements

Height and weight were measured in the subjects when they were in light apparel and without wearing any footwear and BMI was measured by Welcare Accuniq BC 310 fat analyzer.

### Biochemical Estimation

Fasting blood samples were collected and serum was separated after centrifugation at 3000 rpm for 20 minutes. The samples of serum Total T3, Total T4, TSH and hs-CRP were stored for 4 to 6 months at -20ºC. Serum hs-CRP, serum TSH, Total T4 and Total T3 levels were performed using Enzyme Linked Immunosorbent Assay Method (ELISA).

## RESULTS

The total number of subjects were 100 consisting of 78 females and 22 males.

**Table 1: Descriptive Statistics Showing Mean and SD of all Parameters**

| | | n | Minimum | Maximum | Mean ± SD |
|---|---|---|---|---|---|
| AGE (in years) | Non-obese | 22 | 20 | 59 | 37.27 ± 12.31 |
| | Obese | 78 | 19 | 60 | 38.08 ± 11.17 |
| TOTAL T3 (ng/ml) | Non-obese | 22 | 0.99 | 1.69 | 1.41 ± 0.18 |
| | Obese | 78 | 0.96 | 1.91 | 1.36 ± 0.20 |
| TOTAL T4 (µg/ml) | Non-obese | 22 | 5.99 | 10.6 | 8.11 ± 1.55 |
| | Obese | 78 | 5.41 | 10.6 | 8.25 ± 1.38 |
| TSH (mIU/L) | Non-obese | 22 | 4.36 | 8.75 | 6.01 ± 1.06 |
| | Obese | 78 | 4.17 | 9.72 | 7.24 ± 1.65 |
| HEIGHT (in cm) | Non-obese | 22 | 152.4 | 180 | 167.8 ± 6.34 |
| | Obese | 78 | 149.8 | 175.2 | 161.32 ± 6.37 |
| WEIGHT (in kg) | Non-obese | 22 | 57.1 | 77.7 | 66.6 ± 5.50 |
| | Obese | 78 | 59.7 | 87.4 | 69.66 ± 5.94 |
| BMI ($kg/m^2$) | Non-obese | 22 | 21.8 | 24.9 | 23.59 ± 0.85 |
| | Obese | 78 | 25 | 32.2 | 26.75 ± 1.43 |
| hs-CRP (mg/L) | Non-obese | 22 | 3.25 | 8.07 | 5.21 ± 1.34 |
| | Obese | 78 | 2.32 | 8.72 | 5.21 ± 1.72 |

**Table 2: Pearson Correlation between TSH, hs-CRP and BMI in Non-Obese Subjects**

| Non-Obese (n=22) | | | | |
|---|---|---|---|---|
| | | TSH | hs-CRP | BMI |
| TSH | Correlation coefficient | 1 | 0.2672 | -0.0889 |
| | Sig.(2-tailed) | | 0.2293 | 0.6937 |
| hs-CRP | Correlation coefficient | 0.2672 | 1 | -0.0312 |
| | Sig.(2-tailed) | 0.2293 | | 0.8902 |
| BMI | Correlation coefficient | -0.0889 | -0.0312 | 1 |
| | Sig.(2-tailed) | 0.6937 | 0.8902 | |

**Table 3: Pearson Correlation between TSH, hs-CRP and BMI in Obese Subjects**

| Obese (n=78) | | | | |
|---|---|---|---|---|
| | | TSH | hs-CRP | BMI |
| TSH | Correlation coefficient | 1 | 0.455* | 0.341** |
| | Sig.(2-tailed) | | <0.001 | 0.002 |
| hs-CRP | Correlation coefficient | 0.455** | 1 | 0.212* |
| | Sig.(2-tailed) | <0.001 | | 0.06 |
| BMI | Correlation coefficient | 0.341** | 0.212* | 1 |
| | Sig.(2-tailed) | 0.002 | 0.06 | |

**Correlation is highly significant at the 0.01 level (2-tailed) p-value <0.05. *Correlation is significant at the 0.05 level (2-tailed). P-value. Correlation is nonsignificant at p value >0.05.

## DISCUSSION

Globally, Subclinical hypothyroidism (SCH) is the most prevalent endocrine condition [11]. It is characterized with normal total or free T4 and T3 concentrations along with a high Thyroid Stimulating Hormone (TSH) level [2]. It is a clinical condition that characterizes the thyroid gland's activity as slightly decreased, with either little or no hypothyroidism symptoms [12]. Due to its high frequency, potential for developing into

clinical hypothyroidism in the future, and correlation with both direct and indirect CVD risk factors, SCH is clinically significant [13]. As a predictor for future cardiovascular events, hs-CRP directly contributes to the pathophysiology of atherosclerosis by activating endothelium and coronary artery smooth muscle cells [6]. Our study was conducted in Department of Biochemistry, SMS&R with 100 SCH subjects consisting of 78 females and 22 males. The mean ± SD of age group was 37.90 ± 11.50, out of 100 subjects, 85% were of more than 25 years of age. According to the Indian Thyroid Society, the baseline of TSH in SCH is 4.5 to 10 mIU/L [3]. In our study the mean of serum TSH is 6.01±1.06 mIU/L in non-obese and 7.24±1.65 mIU/L in obese in SCH subjects. Glycosylation of TSH is necessary for proper bioactivity. More than hormone release, TRH affects TSH glycosylation.

Low levels of TRH may cause TSH to be less effective, which would lead to inadequate glycosylation. Additionally, TRH alters the thyrotroph's susceptibility to the negative feedback of thyroid hormones. The thyrotroph is more susceptible to negative feedback when TRH levels are dropping, but less susceptible to inhibition when TRH levels are rising. The thyrotroph's thyroid receptors gene expression decreases in response to TRH stimulation, which is the mechanism behind TRH control. TSH release is amplified when the thyrotroph is less susceptible to the thyroid hormone's negative feedback loop. TSH secretion thus rises in response to a drop in thyroid hormone and falls in response to an excess of thyroid hormone. TSH and fT4 have an inverse logarithmic connection; a 50% decrease in fT4 concentration causes a 100-fold increase in TSH [14]. The study shows the mean of serum hs-CRP is 5.21± 1.34 mg/L in non-obese and 5.21±1.72 mIU/L in obese in SCH subjects. The elevated levels of hs-CRP in hypothyroidism are caused by the interaction between IL-6 and TNF-α and IL-1.

The rate of hs-CRP clearance may be hampered by low thyroid hormone levels, which could be one of the causes of the rise in serum hs-CRP levels. Similarly, this phenomenon may also be exacerbated by sluggish hs-CRP uptake in target cells. The low-grade inflammation that may be responsible for the hypothyroidism-related elevated risk of CVD [15]. Vyakaranam S et al (2018), Panchal M, et al (2019), reported that increased hs-CRP values in SCH indicate inflammation as a potential mediator between cardiovascular disease and subclinical hypothyroidism [2,16]. Kumar P, et al (2018) in their study found that when comparing the patient group to the control group, the BMI was significantly greater. The TSH and hs-CRP levels in the patient group were positively correlated. It was a very substantial association [17]. Similar reports have been concluded in the present study that the hs-CRP is positively correlated with serum TSH with the r value 0.4554 & p value <0.001 in subclinical hypothyroidism subjects in Western U.P. region of India.

In present study, 78% subjects were obese whose mean ± SD is 26.75 ± 1.43. Important factors that influence energy consumption and hunger include thyroid hormones. White adipose tissue produces a variety of hormones, including leptin, which can influence HPT axis function by affecting the central nervous system to reflect the amount of stored energy. Obesity raises leptin levels, causing the hypothalamus's PVN to produce thyrotropin-releasing hormone (TRH). Additionally, leptin modifies the function of deiodinases, which facilitates the transformation of T4 into T3. These interactions can cause the thyroid functioning of obese people to differ based on the body's distribution of adiposity [18].

In these circumstances, hypothyroidism, which is characterized by a decreasing basal metabolic rate, may have a significant role in the rise in BMI [19]. Study conducted by Sami A, et al. (2018), Bhat R, et al. (2020) concluded that hypothyroidism and elevated BMI, waist circumference, and waist hip ratio were significantly correlated [20,21]. Similarly, our study concluded that there is significant correlation between BMI and serum TSH in obese subjects with the r value 0.3413 and p value 0.002 respectively, in cases of subclinical hypothyroidism. Lavanya K, Ramamoorthi K, et al in 2017 in their study found that in overweight and obese individuals the mean hs-CRP levels were higher compared to those with normal BMI, there was a positive correlation between BMI and hs-CRP [22]. In the present study, concluded that hs-CRP is non-significant positively correlated with BMI with the r value 0.2129 and p value 0.061 in subclinical hypothyroidism subjects.

## CONCLUSION

It is concluded that there is a significant correlation between hs-CRP and TSH in patients with subclinical hypothyroidism. For SCH patients, elevated levels of hs-CRP are risk factors for the development of CVD. Early recognition of these cases may help to prevent the progression of SCH to overt hypothyroidism. There is significant correlation between BMI and SCH. Elevated TSH levels are associated with both obesity and overweight. Gaining weight along with early thyroid function test screening will help in managing obesity. Regular physical activity, balanced diet, and healthy lifestyle, performing regular yoga may protect overall health and in prevention of obesity and its associated health complications.

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