Xi'an Shiyou Daxue Xuebao (Ziran Kexue Ban)/
Journal of Xi'an Shiyou University, Natural Sciences Edition
ISSN: 1673-064X
E-Publication: Online Open Access
Vol: 67 Issue 03 | 2024
DOI: 10.5281/zenodo.10877591

HIGH-SENSITIVITY C-REACTIVE PROTEIN (hs-CRP) AND SUBCLINICAL HYPOTHYROIDISM (SCH): AN UPDATE

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Abstract

hs-CRP, an acute phase protein and a biomarker of inflammation. It is an indicator of future cardiovascular events. Elevated hs-CRP levels are seen with hypothyroidism. The relation between hs-CRP and SCH, is discussed in the latter part. SCH, defined by elevated thyroid-stimulating hormone levels as per the Indian Thyroid Society Patients diagnosed with SCH, TSH levels is 4.5–10 mIU/L, may progress to overt hypothyroidism. Considering that the condition is subclinical, a significant percentage of the population goes undiagnosed. It is necessary to implement health campaigns to identify these patients at an early stage.

INTRODUCTION

The liver produces an acute-phase protein called hs-CRP in reaction to long-term inflammatory conditions and infections. hs-CRP is an indicator of future cardiovascular events and likely directly contributes to the pathophysiology of atherosclerosis through the stimulation of coronary artery smooth muscle cells and endothelial cells **(1)**.

Since the 1990s, a number of large observational studies have showed hs-CRP, a biomarker of inflammation, as an independent predictor for CAD **(2)**. Endothelial dysfunction is ultimately caused by increased monocyte mobilization into arterial plaque induced by hs-CRP, which suppresses basal and causes nitric oxide release from vascular endothelium. It has been discovered that exposure to hs-CRP causes human coronary artery endothelial cells and systemic vascular endothelial cells to develop more plasminogen activator inhibitor-1 and other adhesion molecules. Furthermore, the hs-

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CRP enhances the absorption of low-density lipoprotein-cholesterol by macrophages. hs-CRP has a direct impact on the atherosclerotic function in vessels **(3)**.

Since inflammation is a component of both acute and chronic atherosclerotic processes, hs-CRP measurements reveal that CRP concentrations are above healthy values but below those observed in infections, indicating that CRP may be a marker of the atherosclerotic process **(4)**.

The American Heart Association and the U.S. Centers for Disease Control and Prevention have designated the following cardiovascular risk categories for hs-CRP values. Risk categories: mild: < 1.0 mg/L, moderate: 1.0–3.0 mg/L, severe: > 3.0 mg/L **(5)**.

Several low-grade immune markers have been found to be elevated in hypothyroidism, including hs-CRP. Roy et al.'s research indicates that Low-level inflammation develops in the early stages of hypothyroidism and raises hs-CRP **(6)**. Syamsunder et al.'s study on sympathetic vagal imbalance in SCH indicates that low-grade inflammation is associated with hs-CRP and is characterized by concurrently elevated sympathetic and decreased vagal activity **(7)**.

Subclinical Hypothyroidism (SCH)

SCH is defined as an increased serum Thyroid Stimulating Hormone level along with normal total or free T4 and T3 levels **(8)**. Patients with SCH are classified into two groups, according to the Indian Thyroid Society: those with a significantly elevated serum TSH level (>10 mUI/L) and those with a moderate elevated TSH level (4.5–10 mIU/L) **(9)**.

According to reviews, prevalence of hypothyroidism was 3.9% and SCH was 9.4%, women were more likely to develop these conditions (11.4%) than men (6.2%). Furthermore, it was found that as people aged, the prevalence of SCH increased. According to a study, SCH, the most common thyroid condition among the elderly, affects 7%–10% of women who are 60 years of age or older **(10)**. It has been shown that 2-5% of cases of SCH may develop into overt hypothyroidism each year **(11)**. As opposed to being a clinical condition, SCH is a biochemical condition because people who have it typically exhibit asymptomatic or non-specific overt hypothyroidism symptoms **(12)**.

It is the initial stage of hypothyroidism, and a thorough medical history, careful examination, and pertinent testing can all be used to diagnose it. Because it doesn't have any symptoms, diagnosis is tough. However, thyroid function testing is widely available, which makes it possible to identify cases of subclinical hypothyroidism early. Early care can also prevent hypothyroidism from progressing to overt hypothyroidism **(13)**.

An update is to show the correlation between SCH and significant conditions such as obesity, metabolic syndrome (MeS), and polycystic ovarian syndrome (PCOS) is currently being prepared. It would also discuss the additional role of hs-CRP plays in these conditions.

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Subclinical Hypothyroidism and Obesity: - Thyroid dysfunction and obesity are two prevalent clinical disorders that have a strong correlation. Hypothyroidism is linked to lower metabolic rate, less thermogenesis, increased BMI, and a higher prevalence of obesity **(14)**. Research conducted by Santa-P R et al., (2022) and other has demonstrated that individuals with abdominal obesity possess greater concentrations of inflammatory markers, such as hs-CRP, in comparison to those of normal weight. Probably rise in fat deposition predisposes to the chronic low-grade inflammation **(15)**. Among the several hypotheses explaining the rise in TSH levels linked to obesity, one possibility is that leptin is responsible for the increased generation of prothyrotropin-releasing hormone. Furthermore, a reduced in T3 receptors in the hypothalamus may contribute to a decrease in peripheral deiodinase activity and feedback **(16)**. It has been observed that there is elevation of serum hs-CRP levels in abdominal obese children as well as in adolescents as compared to normal non-obese subjects. Therefore, the rise in hs-CRP in obese young generation in relation to obesity may precipitate to CVD in older age **(17)**.

Subclinical Hypothyroidism and Metabolic syndrome: - Patients with MetS commonly have elevated levels of the acute phase protein hs-CRP. Previous studies have indicated a strong correlation between elevated levels of hs-CRP and metabolic disorders. Blood pressure, lipid and glucose metabolism, and energy homeostasis are all significantly impacted by thyroid hormones. Thus, it is suggested that functional alterations in the thyroid gland may be linked to MetS and its associated factors, such as obesity, abnormalities in lipid and glucose metabolism, hypertension and insulin resistance (IR) **(18)**.

Subclinical Hypothyroidism and Polycystic Ovarian Syndrome (PCOS): - Among women in the reproductive age group, PCOS is one of the most prevalent and is associated with a variety of disorders, including obesity, metabolic syndrome, insulin resistance, and hyperandrogenism. Women are more likely than men to develop thyroid problems, which can affect menstruation and reproduction. Patients with PCOS typically experience thyroid gland disorders, with 5% to 10% of PCOS patients having SCH **(19)**. According to some summaries, PCOS is a condition of persistent low-grade inflammation that is primarily marked by a slight increase in serum CRP in comparison to weight-matched controls. Low grade chronic inflammation, which is indicated by consistently elevated serum hs-CRP, is an independent marker of CVD **(20)**.

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SUMMARY OF THE STUDIES

S.no.	Study	Conclusion
1.	Nitha NS et al., 2023	In older adults with elevated TSH levels, SCH has been associated with a higher risk of CVD.
2.	Makwane H et al.,2020	According to the study, thyroid function may be one of the main variables influencing body weight and, consequently, obesity. Weight gain in conjunction with early thyroid function test screening will help manage obesity and give obese people early intervention.
3.	Fatima M et al., 2020	According to this study, PCOS and SCH are significantly correlated. SCH may decrease insulin resistance; as a result, thyroid profile screening is necessary for PCOS patients.
4.	Dey A et al., 2019	Subclinical hypothyroidism is associated with elevated hs-CRP, independent of other cardiac risk factors. Patients frequently have dyslipidemia, which is a significant cardiac risk factor. Early SCH diagnosis and treatment may have benefits for cardioprotection.
5.	Panchal M et al.,2019	Elevated hs-CRP levels were more common in our study's subclinical hypothyroid patients. Elevated hs-CRP levels in SCH suggest that inflammation may be the cause of the connection between SCHand CVD.
6.	Kumar P et al., 2018	Elevated hs-CRP and dyslipidemia were observed in SCH patients with TSH <10 μIU/ml. In SCH patients, elevated lipoprotein ratios and hs-CRP may encourage low-grade inflammation, which can lead to the development of cardiovascular risk.
7.	Lavanya K et al.,2017	The significant correlation between hs-CRP and obesity and overweight suggests that obesity is a state of chronic inflammation. As a result, hs-CRP levels can be used to predict future morbidity risk. Given that obesity has become more common in India in recent years and that obesity has a significant negative influence on the nation's healthcare and socioeconomic sectors, hs-CRP can be used to determine the risk of obesity-related disorders in order to initiate early intervention.
8.	Syamsunder, A. N. etal., 2014	SVI in SCH is caused by sympathetic activation and vagal withdrawal, and it progressively rises from SCH to OH. Low-grade inflammation and dyslipidemia are linked to an increased risk of CV and SVI in hypothyroidism.

CONCLUSION

The relation between hs-CRP and SCH is the article's primary focus. Research revealed that patients with subclinical hypothyroidism had elevated levels of hs-CRP. Numerous major CVDs are linked to hs-CRP. Furthermore, SCH is a biochemical disorder that may lead to clinical conditions such obesity, polycystic ovarian syndrome (PCOS), and metabolic syndrome. Early identification and treatment of subclinical hypothyroidism may recognize in the progression of SCH to clinical hypothyroidism, and it may also identify and lower the several cardiac risk factors associated with the condition. As the condition is subclinical, a significant portion of the population remains undetected. Health programs must be conducted in order to identify these patients at an early stage.

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