



IS CRP A SENSITIVE INDICATOR OF CARDIOMETABOLIC RISK IN HYPERTHYROIDISM?

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Abstract

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The present study was undertaken to evaluate the change of C-reactive protein (CRP) concentrations and sensitivity of C-reactive protein (CRP) towards cardio metabolic risk in patients with hyperthyroidism. We studied 75 adult patients with hyperthyroidism and 75 age- and sex-matched euthyroid controls. All hyperthyroid patients were treated with 1 of 2 antithyroid drugs and were reevaluated after thyroid function normalized. Before antithyroid treatment, the hyperthyroid group had significantly higher CRP plasma concentration (mean +/- standard error of the mean, 18.56±11.9 mg/L) than the control group (3.72±1.04 mg/L, P = < 0.001); but the CRP levels dropped significantly after treatment (4.0±1.44 mg/L, P < .001). Blood sugar levels were significantly raised (p<0.001) in hyperthyroid patients as compared to controls. Blood urea and serum Na⁺ & K⁺ levels did not show significant changes when compared to controls. TC, VLDL-C, Tg, LDL-C, AI were significantly decreased in hyperthyroid patients as compared to controls (p<0.001).

There was positive correlation of CRP with TSH, whereas correlation of CRP with T3 and T4 was found to be negative which was significant ($p < 0.001$). The results indicated that plasma CRP concentration was elevated in hyperthyroidism due to inflammation of thyroid gland. The thyroid gland is related to dyslipidemia which is turning related with cardio metabolic risk in thyroid disorders.

INTRODUCTION

Acute thyroiditis, an infection of thyroid, may have features of thyrotoxicosis or hypothyroidism depending on the phase of the illness.¹ C-reactive protein is an abnormal protein that appears in blood in various inflammatory disorders. At present, the CRP test is accepted as a valuable aid in the diagnosis of low grade, questionable rheumatic fever, in following the course of this disease during treatment and in the differential diagnosis of coronary insufficiency.²

CRP levels invariably rise after major surgery but during postoperative period they fell towards normal in 7-10 days.³ that's why CRP can be a sensitive indicator of cardio metabolic risk in hyperthyroid patients.

PATIENTS & METHODS

75 age and sex matched controls and 75 patients of thyroid disorders admitted to wards or attending OPD's of Pt. B. D. Sharma PGIMS, Rohtak. Only clinically diagnosed cases were included in the study. Pregnant women, patients on thyroxine, oral contraceptives, Lipid lowering agents, rheumatoid arthritis patients, coronary artery disease, thyroidectomy patients were excluded from the study.

RESULTS AND DISCUSSION

A series of biochemical measurements of Blood Glucose(Glucose oxidase-Peroxidase)⁴ , Blood Urea (Diacetyl Monoxime)⁵, Serum Sodium & Potassium (Fp20)⁶,Lipid profile(Cholesterol oxidase peroxidase)⁷,HDL-Cholesterol(Cholesterol oxidase peroxidase)⁸, Serum Triglyceride(Lipase)⁹,VLDL-Cholesterol¹⁰ were performed by respective methods.

Results of a thorough medical examination and T_3 (RIA)^{11,12}, T_4 (RIA)^{13,14}, TSH(IRMA)^{15,16}, CRP(Turbidimetric)^{17,18} were carried out. Regarding the clinical investigation, T_3 equal or above 200 ng/dl was considered Hyperthyroidism. T_4 values of serum exceeding 13.5 μ g/dl were considered hyperthyroidism and vice versa. Serum TSH levels below 0.17 μ U/ml were considered to be Hyperthyroidism. CRP levels above 6mg/L were considered to be high. Data analysis was performed by student t-test and correlation between variables was studied by using Pearson's correlation coefficient test. The level of significance was set at $p < .0001$.

Table1 shows the various routine biochemical investigations in controls and hyperthyroid patients. Blood sugar levels were significantly raised ($p < 0.001$) in hyperthyroid patients as compared to controls. Blood urea and serum Na^+ & K^+ levels did not show significant changes when compared to controls. TC, VLDL-C, Tg, LDL-C, AI were significantly decreased in hyperthyroid patients as compared to controls($p < 0.001$).

COMPARISON OF CRP LEVELS BEFORE AND AFTER TREATMENT

TABLE-2 shows levels of CRP in patients and controls. The levels of CRP before treatment were significantly higher in hyperthyroid patients as compared to those of the controls ($p < 0.001$).

COEFFICIENT OF CORRELATION (r) OF CRP WITH T_3 , T_4 , TSH

Table-3 shows that there was positive correlation of CRP with TSH, whereas correlation of CRP with T_3 and T_4 was found to be negative which was significant.

DISCUSSION

The objective of this study was to assess the cardio metabolic risk in hyperthyroid patients. The association of thyroid disorders and CRP levels has been the area of interest in the recent past. In subclinical hyperthyroidism with serum TSH levels < 0.1 mIU/L, the incidence of AF is increased, and in overt hyperthyroidism, cardio embolic stroke is clearly associated to thyrotoxic AF. There is insufficient evidence to support the concept of an increased cardio embolic risk attributable to a hypercoagulability state. Only in vivo and in vitro studies suggest an

increased thrombotic risk in thyrotoxicosis.¹⁹

Hyperthyroidism is associated with atrial fibrillation and cardio embolic stroke. Hypothyroidism is associated with a worse cardiovascular risk factor profile and leads to progression of atherosclerosis. Associations between hyperthyroidism and acute cerebral venous thrombosis, Moyamoya, and Giant cell arthritis have been suggested, but sound evidence is lacking. Additional studies are needed to clarify this issues.²⁰

Thyroid disease is related to the development of dyslipidemia which is a well-known atherogenic factor. Dyslipidemia induces insulin resistance oxidative stress, via a vice-vicious cycle.²⁵⁻³⁰ Insulin resistance, hypertension, inflammation, oxidative stress, and coagulation deficits are also promoted by thyroid disease, independently of dyslipidemia.²¹⁻²⁴ The above associations support a multifactorial origin of atherosclerosis in thyroid disease, with dyslipidemia playing an important role.²¹⁻²⁴ clinical hyperthyroidism has been associated with systolic hypertension,

increased pulse pressure, and possibly hyperhomocysteinemia.²³⁻²⁴ Additionally, patients with overt hyperthyroidism have a hypercoagulable state and an increased risk of thrombosis.³² Higher levels of homeostasis model assessment and lower levels of Matsuda indexes have been reported, suggesting insulin resistance.³¹⁻³⁵ Decreased fractional postprandial glucose uptake in adipose tissue, increased fasting lipolysis, increased interleukin 6, and tumour necrosis factor alpha may be associated to its development.^{31,35}

CONCLUSION

We observed significantly increased CRP levels in Hyperthyroid patients to 18.56 ± 6.69 mg/L ($p < 0.001$) as compared to controls. Two months after treatment CRP levels were significantly decreased to 4.0 ± 1.44 mg/L in hyperthyroid patients as compared to controls. Crain et al measured CRP levels which were higher in hypothyroidism when compared with controls. CRP, an acute phase protein which circulates in higher concentrations in a variety of acute and chronic disease states.⁴⁰

Low grade inflammation is the most common cause of thyroid disorders. CRP levels were elevated because of inflammation of thyroid gland in patients of

hypothyroidism and hyperthyroidism. The low levels were because of decreased inflammation of thyroid gland after treatment.

Table 1.

| PARAMETERS | CONTROLS (MEAN±SD) | HYPERTHYROID CASES (MEAN±SD) | P VALUE |
|-------------------------------|-----------------------|---------------------------------|---------|
| T ₃ (ng/dl) | 129.3±30.9 | 316±153 | <.001 |
| T ₄ (µg/dl) | 7.9±1.9 | 16.2±7.9 | <.001 |
| TSH(µIU/ml) | 2.5±1.0 | 0.105±0.01 | <.001 |
| Blood Glucose(mg/dl) | 135.2±7.3 | 142.55±11.87 | <.001 |
| Blood Urea(mg/dl) | 30.0±4.7 | 31.06±4.9 | NS |
| Serum Na ⁺ (meq/l) | 138.18±6.1 | 132.27±3.8 | NS |
| Serum K ⁺ (meq/l) | 3.9±0.6 | 3.74±0.4 | NS |
| TC(mg/dl) | 171.6±26.2 | 127.4±20.4 | <.001 |
| HDL-C(mg/dl) | 37.8±6.1 | 51.5±2.7 | <.001 |
| TG(mg/dl) | 128.1±37.3 | 103.6±26.2 | <.001 |
| VLDL-C(mg/dl) | 25.6±8.2 | 20.7±5.2 | <.001 |
| LDL-C(mg/dl) | 108.2±20.9 | 55.2±22.6 | <.001 |
| AI | 3.5±0.4 | 1.24±0.29 | <.001 |

TABLE-2

| GROUP | CRP LEVELS BEFORE TREATMENT(MEAN±SD) mg/L | CRP LEVELS AFTER TREATMENT(MEAN±SD) mg/L | P value |
|--------------|---|--|---------|
| HYPERTHYROID | 18.56±11.9 | 4.0±1.44 | <0.001 |
| CONTROLS | 3.72±1.04 | ----- | <0.001 |

TABLE-3

| PARAMETER | CRP |
|----------------|-----------|
| T ₃ | r=0.366* |
| T ₄ | r=0.424* |
| TSH | r=0.438** |

*Negative significant correlation at the 0.01 levels

** Positive significant correlation at the 0.01 levels

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