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Research Article

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C-reactive protein as an additional marker for increased risk of cardiovascular disease in patients of hypothyroidism

Pooja S. K. Rai¹*, Supriya Dawri¹, Smita A. Deokar¹, Shimi Sundharan¹, Sudarshan Shelke¹, Amruta A. Bakshi², Anita B. Rai³

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*Correspondence:

Dr. Pooja S. K. Rai,

E-mail: poojaonline21@gmail.com

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ABSTRACT

Background: Prevalence of hypothyroidism and its subsequent cardiometabolic complications is on exponential rise. CRP is raised in hypothyroid patients long before other metabolic derangements of hypothyroidism take place and may be a common Patho physiological factor tying together various components of cardiometabolic dysfunction. Present study was aimed at evaluating the role of CRP as an additional cardiovascular risk marker in hypothyroid patients.

Methods: 46 diagnosed hypothyroid patients and 46 age and sex matched healthy controls were included in this study. Participants were evaluated based on detailed history, clinical examination and laboratory investigations. Blood samples were collected after overnight fast. Serum T₃, T₄, TSH, Total Cholesterol (TC), Triglycerides (TG), HDL Cholesterol (HDL-C), VLDL Cholesterol (VLDL-C), LDL Cholesterol (LDL-C) and CRP were estimated. Results were analyzed by unpaired t-test, P-value was determined & Correlation coefficient was calculated amongst various parameters.

Results: Statistically significant increased levels of serum TSH, total cholesterol, triglycerides, HDL cholesterol, LDL cholesterol and CRP in hypothyroid patients as compared with control were observed. We found decreased levels of serum T₃ and T₄ in hypothyroid patients as compared with control.

Conclusions: An atherogenic lipid profile along with inflammation in patients with hypothyroidism predispose them to cardiovascular disease. Study suggests CRP; a simple, sensitive & independent cardiovascular risk predictor in hypothyroid patients with a potential to reveal hidden burden of metabolic dysfunction and offers a hope that, cardiovascular event can be well prevented with appropriate interventions.

Keywords: Lipid Profile, Hypothyroidism, CRP

INTRODUCTION

Thyroid hormones play an important role in maintaining metabolic homeostasis in adults. Hypothyroidism is a known risk factor for Coronary Vascular Disease (CVD) which may in part be due to dyslipidemia seen in

hypothyroidism.^{1,2} C-Reactive Protein (CRP), an acute phase reactant whose levels increases in inflammatory conditions has now evolved into an independent risk marker for atherosclerosis and CVD.³ Many studies have shown CRP levels rises in hypothyroidism and may count as additional risk factor for development of coronary

¹Department of Biochemistry, Lokmanya Tilak Municipal Medical College & General Hospital, Sion, Mumbai, Maharashtra, India

²Department of Biochemistry, Terna Medical College and Hospital, Mumbai, Maharashtra, India ³Department of Microbiology, B.N. Bandodkar College of Science, Thane, Maharashtra, India

heart disease in such patients.⁴ The current study is aimed to evaluate the levels of CRP and serum lipid profile in hypothyroid patients.

METHODS

This study was conducted in the department of biochemistry and medicine, at Pandit Bhagwat Dayal Sharma, Rohtak. Approval from institutional ethical committee was taken.

46 hypothyroid cases and 46 age and sex matched euthyroid controls were taken for this study. Serum T₃ (by radioimmunoassay),^{5,6} T₄ (by radioimmunoassay)^{7,8} and TSH (by immunoradiometric assay)^{9,10} total cholesterol (Cholesterol oxidase - peroxidase),¹¹ triglycerides (Glycerol kinase, glycerol oxidase peroxidase),¹² HDL cholesterol (Polyanionic Precipitation),¹³ VLDL cholesterol & LDL cholesterol (Calculated by Friedwald's Formula)¹⁴ were estimated. CRP was measured by turbidimetric method. ^{15,16} Pregnant women, patients on thyroxine, oral contraceptives, statins, patients with a history of rheumatoid arthritis, coronary artery disease, any other acute or chronic inflammatory conditions and patients who have undergone thyroidectomy were excluded from this study.

RESULTS

Table 1 shows a significantly (P <0.001) decreased levels of T_3 in the hypothyroid patients (53.8 \pm 34.1 ng/dl) as compared to the healthy controls (129.3 \pm 30.9 ng/dl). T_4 levels were also significantly (P <0.001) decreased in the hypothyroid patients (2.0 \pm 1.5 μ g/dl) as compared to the healthy controls (7.9 \pm 1.9 μ g/dl). There were also a significant (P <0.001) increase levels of TSH in the hypothyroid patients (89.5 \pm 24.5 μ IU/ml) as compared to the healthy individuals (2.5 \pm 1.0 μ IU/ml).

Table 1: Comparison of thyroid profile in hypothyroid cases and controls.

Parameters	Control (mean ± SD) n=46	Hypothyroid patients (Mean ± SD) n=46	P value
T ₃ (ng/dl)	129.3 ± 30.9	53.8 ± 34.1	<0.001*
$T_4 (\mu g/dl)$	7.9 ± 1.9	2.0 ± 1.5	<0.001*
TSH (µIU/ml)	2.5 ± 1.0	89.5 ± 24.5	<0.001*

^{*}P value statistically significant

Table 2 shows a significantly (p < 0.001) increased levels of TC in the hypothyroid patients (280.75 \pm 18.9 mg/dl) as compared to the healthy controls (171.6 \pm 26.2 mg/dl). TG levels were also significantly (P <0.001) increased in the hypothyroid patients (151.6 \pm 26.7 mg/dl) as compared to the healthy controls (128.1 \pm 37.3 mg/dl). There were also a significant (P <0.001) increase levels

of HDL-C in the hypothyroid patients (44.3 \pm 5.6 mg/dl) as compared to the healthy individuals (37.8 \pm 6.1 mg/dl).

VLDL-C levels were also significantly (P <0.001) increased in the hypothyroid patients ($30.3 \pm 5.7 \text{ mg/dl}$) as compared to the healthy controls ($25.6 \pm 8.2 \text{ mg/dl}$). There were also a significant (P <0.001) increase levels of LDL-C in the hypothyroid patients ($206.5 \pm 20.1 \text{ mg/dl}$) as compared to the healthy individuals ($108.2 \pm 20.9 \text{ mg/dl}$). The CRP levels were also significantly (P <0.001) increased in the hypothyroid patients ($28.38 \pm 11.9 \text{ mg/L}$) as compared to the healthy individuals ($3.72 \pm 1.04 \text{ mg/L}$).

Table 2: Comparison of serum lipid profile and CRP in hypothyroid cases and controls.

Parameters	Control (mean ± SD)	Hypothyroid patients (Mean ± SD)	P value
Total cholesterol (mg/dl)	171.6 ± 26.2	280.75 ± 18.9	<0.001*
Triglycerides (mg/dl)	128.1 ± 37.3	151.6 ± 26.7	<0.001*
HDL cholesterol (mg/dl)	37.8 ± 6.1	44.3 ± 5.6	<0.001*
VLDL cholesterol (mg/dl)	25.6 ± 8.2	30.3 ± 5.7	<0.001*
LDL cholesterol (mg/dl)	108.2 ± 20.9	206.5 ± 20.1	<0.001*
CRP (mg/L)	3.72 ± 1.04	28.38 ± 11.9	<0.001*

^{*}P value statistically significant

DISCUSSION

We found statistically significant increase in serum TSH, total cholesterol, triglycerides, HDL cholesterol, LDL cholesterol, VLDL cholesterol and CRP in hypothyroid patients when compared with control. We found decreased levels of serum T_3 and T_4 in hypothyroid patients compared with control.

In hypothyroidism, increased total cholesterol is due to the decreased catabolism and increased levels of serum cholesterol. The catabolism of cholesterol into bile is mediated by the enzyme cholesterol 7α -hydroxylase. This liver-specific enzyme is negatively regulated by T_3 and may contribute to hypercholesterolemia. Increase in LDL cholesterol is due to decreased expression of LDL receptors causing decreased clearance of LDL from circulation.

Levels of adipose tissue lipoprotein lipase (LPL) and hepatic lipase results in increased circulating triglycerides and VLDL.¹⁹

Decreased hepatic lipase and cholesterol-ester transport protein (CETP) results in decreased catabolism of HDL, reduced transport of cholesteryl esters from HDL $_2$ to Very Low-Density Lipoproteins (VLDL) and Intermediate Density Lipoprotein (IDL), reduced transport of HDL $_2$ to HDL $_3$ ²⁰ and thus increased levels of HDL $_2$. ^{18,19}

Increase in serum CRP levels can be due to inflammatory disorders of thyroid gland resulting in hypothyroidism. Thus CRP can be used as an early marker to prevent cardiovascular events in hypothyroidism for proper interventions and treatment.

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Ethical approval: The study was approved by the

institutional ethics committee

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