Original Research Article

Circulatory levels of HsCRP in non-alcoholic fatty liver disease

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Abstract

Background: Non-alcoholic fatty liver disease (NAFLD) is the most prevalence cause of cardio mortality due to subclinical inflammation. Various factors play an important role in setting the subclinical inflammation. Job profile extended working hours, sedentary life style, and unhealthy dietary habits as well modulation of genetic factors make NAFLD as one of the leading underlying causes or the result of various diseases. It is mainly characterized by abnormal deposition of fat in liver followed by production of inflammatory mediators. HsCRP is one of the proinflammatory mediators which indicate the level of inflammation. HsCRP is also identified as one of the cardiac marker. The pathophysiology of NAFLD is not fully understood, although it is often related to insulin resistance, Diabetes and Cardiovascular complications. **Aim:** The aim of this study was to evaluate the circulatory levels of HsCRP in patients of non-alcoholic fatty liver disease and compare them with clinically healthy controls. Results: The present study observed a significant increase anthropometric parameters and lipid parameters in patients than controls. TG and LDL have shown an increased pattern in circulatory levels in serum. Abnormal lipid profile reported high TG and LDL in patients than controls, TG [158.22 (±80.11)/ 110.68 (±43.21)] and LDL [120.16 (±45.32)/ 99.30 (±32.80)]. A significant difference was found in circulatory levels of ALT in hypothyroidism patients than controls [46.3(± 3.8) /19.24(± 3.1)]. **Conclusion:** The present study concluded that HsCRP can be considered as an important marker of inflammatory status in NAFLD and NASH.

Key Word: Inflammatory Markers, NAFLD, NASH, HsCRP

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INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is a wide spectrum of diseases ranging from simple steatosis with fat accumulation to steatohepatitis, fibrosis as well cirrhosis or hepatocellular carcinoma[1,2]. Inflammation is the key player in path physiology of most of the diseases. Obesity is known as one of the major risk factor for NAFLD[3]. HsCRP is a potent indicator of subclinical inflammation and plays a crucial role in various inflammatory cascades and may lead to cardiovascular diseases[4]. The human CRP is made up of five identical non-glycosylated polypeptide chains, containing 206 amino acid residues per chain. It is synthesized mainly in liver, however it is also produced at many other sources. CRP and hsCRP are the two names given to the same protein. CRP is measured in a broader range as it is a non specific marker of inflammation and increases in many inflammatory conditions[3,4]. Correlations of C-reactive protein levels with anthropometric profile, percentage of body fat and lipids in healthy adolescents and young adults has been observed in young Indian population[3]. NAFLD is a classical disease due to abnormal deposition of fat in liver and may develop some inflammatory condition which may lead to NASH[5]. For this development inflammation plays a crucial role with many other factors. HsCRP is one of the inflammatory

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molecules identified and shown to be associated with development of NASH. IL-6 is considered to induce hepatic production of the acute phase protein hs-CRP and has been elevated in conditions like obesity, type 2 diabetes mellitus[6,7]. HsCRP has been identified as a culprit in vulnerable atherosclerotic plaques and is associated with ACS[8]. The aim of this study was to evaluate the circulatory levels of HsCRP in patients of non-alcoholic fatty liver dis

METHODOLOGY

The study included 225 NAFLD patients and 220 clinically healthy controls. This study was carried out at Dr. D.Y. Patil Medical College, Nerul, Navi Mumbai. The study information was given to all the study participants and their written consent was collected. The study has been approved by the Institutional Ethics Committee.

Inclusion criteria: Clinically proven NAFLD patients (NAFLD was detected by ultrasound), Age and sex matched healthy individuals control group.

Exclusion criteria: Patient with significant alcohol intake (>20 g/day) type 2 diabetes mellitus (T2DM), cardiovascular disease (CVD), presence of other liver diseases (alcoholic liver disease, viral hepatitis, autoimmune hepatitis, primary biliary cirrhosis, biliary obstruction, drug-induced liver damage etc.), severe end organ damage, human immunodeficiency virus infection, pregnancy and lactation, were excluded from the study

Blood Sampling and Methodology: Fasting venous blood samples were collected for biochemical investigations. Routine biochemical parameters like fasting blood sugar, lipid profile, liver function tests and Serum HsCRP levels were estimated in clinical laboratory of D.Y Patil hospital and research center, Nerul, Navi Mumbai. Cardiac profile is also evaluated by ECG, ECHO findings as well angiographic results. SPSS software (version 17) was used for Statistical analysis of the data.

RESULTS

A total of 90 patients were studied, of which (53%) were male. The body mass index (BMI) for age and sex classified 38 (42.2%) participants as obese and 52 (57.7%) as severe obese. NASH has been identified in 56 (62.2%) participants and approximately 90% of them presented grade I steatosis. TG and LDL have shown an increased pattern in circulatory levels in serum. The lipid profile variables like TG [158.22 (±80.11)/ 110.68 (±43.21)] and LDL [120.16 (±45.32)/ 99.30 (±32.80)] were high patients than controls.

Table 1: Demographical Characteristics of study subjects

Variables	Controls (n=96)	Patients (n=90)	*P* value
BMI	24.34 (±3.90)	30.33 (±5.75)	0.05
WC	94.6 (±10.7)	101.20 (± 12.16)	0.05
WHR	0.96 (±0.59)	1.06(±0.42)	0.01
TG (mg%)	110.68 (±43.21)	158.22 (±80.11)	0.05
TC (mg%)	173.27 (±30.17)	213.34 (±48.64)	0.05
LDL (mg%)	99.30 (±32.80)	120.16 (±45.32)	0.05
ALT(IU/L)	76.3± 10.8	18.4± 3.4	0.01
AST (IU/L)	38.8 ± 4.3	26.2 ± 2.8	0.05

Table 2: Serum HsCRP

Variables	NAFLD	NASH	*P* value
Serum HsCRP	2.13(±0.11)	3.40(±0.58)	0.05

The present study observed a significant increase anthropometric parameters and lipid parameters in patients than controls. The inflammatory marker C-reactive protein levels increased in NASH group than NAFLD.

DISCUSSION

Our study observed high levels of hsCRP in NASH patients than NAFLD. A significant difference was observed in lipid profile and anthropometric measurements of controls and fatty liver patients. The present study supported the hypothesis that hsCRP levels are associated subclinical inflammation associated with fatty liver. Hence hsCRP can be considered as an important marker of inflammatory status in NAFLD and NASH patients. High serum hs-CRP reflects its synthesis is in response to a pathological process[9]. Proinflammatory mediaters like IL-6 and TNF –alpha plays an important role in production of HsCRP in liver. *In vivo* release of interleukin-6 (IL-6), linked closely to hs-CRP pathway. Hence IL-6 levels considered as an important indicator for subclinical inflammation which is broadly specific. Various studies have shown the association of IL-6 with path physiological conditions, like obesity, type 2

diabetes and CVD[6,8].While the pathophysiology of NAFLD is not completely understood, accumulation of triglycerides in hepatocytes is due to various factors like-presence of oxidative stress, lipid peroxidation, pro-inflammatory cytokines (e.g. TNF-α, IL-6)[13]. Further in vivo studies in NAFLD and NASH patients, liver biopsies have revealed hepatic distribution (mRNA) of the inflammatory cytokine TNF-α with its receptors [14].Some studies also observed the adiponectin m-RNAs in liver biopsies of these patients . Further they have noted the apperence of the m-RNAs of adeponectin receptors also[15]. Animal studies showed that increased systemic levels of TNF-α is a result of high amount of fatty acids present in the liver which mediate hepatic production of TNF-α[16]. Hepatocye damage facilitates activation of liver-specific macrophages ('Kupffer Cells') which secretes more TNF-α and IL-6 into the blood[17].

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