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Original Research Article

A Case Control Study to Assess the Circulatory Levels of Hs-CRP in Patients of Non-Alcoholic Fatty Liver Disease: An Observational Study

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Abstract

Aim: The aim of the present study was to evaluate the circulatory levels of Hs-CRP in patients of non-alcoholic fatty liver disease and compare them with clinically healthy controls.

Material & Methods: The study included 100 NAFLD patients and 100 clinically healthy controls. This study was carried out at. The study information was given to all the study participants and their written consent was collected.

Results: The lipid profile variables like TG and LDL were high patients than controls. 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.

Conclusion: The present study concluded that Hs-CRP can be considered as an important marker of inflammatory status in NAFLD and NASH.

Keywords: Inflammatory Markers, NAFLD, NASH, Hs-CRP

Introduction

Non-alcoholic fatty liver disease (NAFLD) encompasses a spectrum of clinic-pathologic entities that have in common the presence of fat accumulation in the liver in the absence of significant alcohol consumption. [1,2] It is characterized by triglyceride accumulation in hepatocytes, which occurs without alcohol abuse. It is one of the most commonly encountered chronic liver diseases. [3] The clinical spectrum of NAFLD ranges from asymptomatic steatosis to steatohepatitis, fibrosis and cirrhosis. Most NAFLD patients have asymptomatic simple steatosis without adverse sequelae. [4] Inflammation is present in the early phase of NAFLD and is an essential driver in the initiation and progression of liver damage. [5]

NAFLD is strongly associated with the major components of the metabolic syndrome. Increasing recognition of the importance of NAFLD and its strong relationship with the metabolic syndrome has stimulated an interest in the possible role of NAFLD in the development of cardiovascular disease (CVD). Mortality is even higher amongst individuals with non-alcoholic steatohepatitis (NASH), and this mortality was primarily cardiovascular, rather than liver related. [6]

Liver is the center for the production of classical biomarkers of inflammation and endothelial dysfunction. Their secretion is partly dependent on factors that are up-regulated in the presence of insulin resistance and the metabolic syndrome. A series of proinflammatory proteins and cytokines are implicated in hepatic inflammation have been studied to test their usefulness as non-invasive soluble biomarkers for NAFLD/NASH diagnosis and prognosis. [7]

IL-6 and TNF-a are the major stimuli responsible for increased hepatic production of C-reactive protein (CRP), fibrinogen and other acute-phase proteins. [8,9] HsCRP is a potent indicator of subclinical inflammation and plays a crucial role in various inflammatory cascades and may lead to cardiovascular diseases. [10] 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. [10,11] 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. [11] NAFLD is a classical disease due to abnormal deposition of fat in liver and may develop some inflammatory condition which may lead to NASH. [12] HsCRP is one of the inflammatory molecules identified and shown to be associated with development of NASH. HsCRP has been identified as a culprit in vulnerable atherosclerotic plaques and is associated with ACS. [13]

Hence the aim of this study was to evaluate the circulatory levels of HsCRP in patients of non-alcoholic fatty liver.

Material & Methods

The study included 100 NAFLD patients and 100 clinically healthy controls. This study was carried out at department of General Medicine, Gouri Devi Institute of Medical Sciences and Hospital, Durgapur, West Bengal, India for one year . The study information was given to all the study participants and their written consent was collected.

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.

Statistical Analysis

SPSS software (version 17) was used for Statistical analysis of the data**.**

Results

Table 1: Demographical Characteristics of study subjects

Variables	Controls (n=100)	Patients (n=100)	*P* value
BMI	23.37 (±3.87)	25.35 (±5.65)	0.07
WC	92.8 (±10.5)	100.22 (± 12.16)	0.07
WHR	0.95 (±0.55)	1.07 (±0.43)	0.01
TG (mg%)	110.68 (±43.21)	158.22 (±80.11)	0.06
TC (mg%)	172.24 (±30.12)	212.38 (±47.63)	0.02
LDL (mg%)	99.30 (±32.80)	120.16 (±45.32)	0.07
ALT(IU/L)	75.5± 10.5	17.3± 3.4	0.01

The lipid profile variables like TG and LDL were high patients than controls.

Table 2: Serum HsCRP

Variables	NAFLD	NASH	*P* value
Serum HsCRP	2.12 (±0.18)	3.43 (±0.57)	0.07

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

Fatty liver is a clinical condition characterized by and commonly understood as the accumulation of lipids within hepatocytes. Traditionally, for practical purposes a, hepatic fat content exceeding 5% of the liver weight has been considered as fatty liver. [14] In the past, fatty liver was well‑thought‑out as a benign and reversible pathology and represented a nonspecific response of the liver to metabolic stress of various origin.[2] However, it is increasingly seen as a part of the spectrum that can be as benign as fatty liver to a fatal condition of hepatocellular carcinoma (HCC). Alcohol consumption has been the most common factor responsible for fatty liver, however, it may also be seen in non‑alcoholics and the clinical entity is known as non‑alcoholic fatty liver disease (NAFLD). It is commonly associated with various components of metabolic syndrome including obesity, diabetes mellitus, and dyslipidemia. [15] Various reports also suggest that NAFLD may be associated with low‑grade inflammation in liver. [16]

The lipid profile variables like TG and LDL were high patients than controls. 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. High serum hs-CRP reflects its synthesis is in response to a pathological process9. 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. [17,18] 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). [19]

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. [20] 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. [21] Hepatocye damage facilitates activation of liver-specific macrophages ('Kupffer Cells') which secretes more TNF-α and IL-6 into the blood. [22] A recent follow‑up study was done by Lee et al [23] to address whether hs‑CRP levels within the normal range can predict the development of NAFLD in healthy male subjects. In the 7‑years follow‑up, it was found that the risk for NAFLD increased as the hs‑CRP level increased ($P < 0.001$). As the hs‑CRP level increased within the healthy cohort, the risk of developing NAFLD increased.

Conclusion

The present study concluded that Hs-CRP can be considered as an important marker of inflammatory status in NAFLD and NASH.

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