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Original Research Article

Study of Serum Hs-CRP & Lipid Profile in Non-Alcoholic Fatty Liver Disease Patients in Tertiary Care Hospital of Central India

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Abstract:

Introduction: Non-alcoholic fatty liver disease (NAFLD) includes a spectrum of liver damage ranging from simple steatosis to non-alcoholic steato hepatitis (NASH), increased liver fibrosis and rarely, progression to liver cirrhosis. It is frequently associated with obesity and metabolic syndrome. Chronic inflammation and altered lipid profile are frequently associated with the metabolic syndrome.

High sensitive C-reactive protein (hs-CRP) an important diagnostic and prognostic marker for many systemic inflammatory diseases, as very low concentrations of CRP can be analyzed in the serum.

High prevalence of NAFLD worldwide causes increased morbidity & mortality & have increased economic burden in the community. Pathogenesis of NAFLD may be associated with the destruction of hepatocytes resulting from immune and inflammatory mediators.

Studies about the role of inflammation in the pathogenesis of NAFLD, shown conflicting and non-conclusive results hence any reliable clue will be considered valuable.

Aims & Objective: To compare the serum levels of hs-CRP and lipid profile in patients of NAFLD and in healthy controls.

Materials and Methods: This cross-sectional study included 50 patients of NAFLD (case group) and 50 age and gender matched healthy subjects (control group). Serum hs-CRP and lipid profile were measured for both the groups.

Results: The mean concentrations of hs-CRP in the case group and the control group were 4.2±1.2 mg/l and 2.2±0.4 mg/l respectively. The difference is statistically significant ($P < 0.05$). In Our study we also found significantly altered lipid parameters in case group than in control group. ($P < 0.05$)

Conclusion: This study has shown that inflammation and alteration in lipid profile is more evident in patients of NAFLD as compared to healthy subjects.

Keywords: Non-alcoholic Fatty Liver Disease, Metabolic Syndrome, Lipid Profile, Inflammation, hs-CRP.

Introduction

Non-alcoholic fatty liver disease (NAFLD) is a clinical term that has been increasingly diagnosed in the last decades and used for a range of conditions caused by a build-up of fat in the liver. Maximum allowable level of alcohol intake for definition of

NAFLD is 2 standard drinks a day (140 g ethanol/week) for men, and one standard drink a day (70 g ethanol/week) for women. [1]

NAFLD includes a spectrum of liver damage ranging from simple steatosis to non-alcoholic steatohepatitis (NASH), increased liver fibrosis and rarely, progression to liver cirrhosis. It is frequently associated with obesity and metabolic syndrome. Metabolic syndrome (MS) is a group of cardiovascular risk factors associated with insulin resistance, hypertension, glucose intolerance, hypertriglyceridemia and low levels of high-density lipoprotein cholesterol (HDL-C). Chronic inflammation is frequently associated with the MS. Proinflammatory cytokines that have been linked with MS include CRP, TNF-α, IL-6 and they result in more insulin resistance, hepatic triglyceride stores and increased VLDL production in liver. Recent studies emphasize the role of proinflammatory cytokines, insulin resistance, oxidative stress and subsequent lipid per oxidation in the development and progression of NAFLD. Pathophysiology of NAFLD still has not been completely cleared. However, insulin resistance plays a fundamental role in the pathogenesis of fatty liver. At the early stage of NAFLD, inflammation of kupffer cells could contribute to hepatic steatosis and recruitment of other immune cells into the liver. IL1β secretion by inflammed kupffer cells promotes accumulation of triglyceride in hepatocytes through the inhibition of peroxisome proliferator-activated receptor alpha (PPARα) mediated fat oxidation. [2]

High sensitivity CRP (hs-CRP) refers to the lower detection limit of the assay procedures being used and is similar to routine CRP in structure and function. It has been suggested that hs-CRP has given an idea about ongoing inflammation and tissue damage very accurately compared to other laboratory parameters of the acute-phase response. The hs-CRP is an important marker of tissue damage and inflammation. It is useful in assessment of severity of inflammation. [3] There are reports that hs-CRP levels are significantly correlated with liver histology in NAFLD patients, suggesting that NAFLD may be associated with low-grade inflammation in the liver. [4]

Due to the increasing prevalence of NAFLD in India, the present study was conducted in central part of India with an objective to evaluate the serum hs-CRP and lipid profile in NAFLD cases and compare them with controls.

Material & Methods

This study was conducted in Department of Biochemistry of M.G.M. Medical College and M.Y.H. Hospital Indore, after approval from institutional ethical committee from July 2018 to July 2019, includes 50 USG confirmed patients of fatty liver with no history of alcohol abuse (NAFLD) were taken as case group and 50 age and gender matched healthy subjects without NAFLD were taken as control group.

Inclusion Criteria:

Subjects with age group 45-65 years and both genders were taken. Cases include patients of NAFLD assessed on imaging and controls included age and gender matched healthy subjects.

Exclusion criteria:

Patients with alcohol consumption >140 gm/week for men and >70gm/week for women, Patients with a history of viral hepatitis, autoimmune hepatitis or other forms of chronic liver disease.

Investigation Procedure:

Venous blood (5 ml) sample was withdrawn with aseptic precautions from the antecubital vein following overnight fasting. The blood sample was collected in clot activator tube and serum was separated. The serum was analysed for biochemical investigations on same day

and remaining samples were preserved for further biochemical investigations at -20°C.

Serum hs-CRP level was estimated by Immunoturbidimetry method using CRP-ULTRA turbinates kit on Biosystem BA400 Biochemistry fully automated analyser. Lipid profile was measured by using fully automated biochemistry analyzer and spectrophotometer.

Data Collection and Statistics: The data were expressed as mean ± standard deviation. SPSS version 20 software was used for statistical analysis. Unpaired Student t test was applied to compare hs-CRP between two groups (control & cases). P values less than 0.05 was considered significant.

Table 1: Comparison of Biochemical parameter between Case & Control

SN	Parameter	Controls (Mean ±S.D.) n=50	Cases (Mean ± S.D.) n=50	p-value
1.	Cholesterol(mg/dl)	174±34	189±40	<0.05
2.	TGs(mg/dl)	126.71±19.48	193.57±99.41	<0.05
3.	HDL (mg/dl)	44±12	38±6.4	<0.05
4.	LDL(mg/dl)	108±32	121±33	<0.05
5.	hs-CRP(mg/l)	2.2±0.4	4.2±1.2	<0.05

P value <0.05 was taken as statistically significant

Results:

The biochemical parameters including lipid profile and hs-CRP of case and control groups are depicted in the Table 1**.** The mean concentrations of hs-CRP in the case group and the control group were 4.2±1.2 mg/l and 2.2±0.4 mg/l respectively. The difference is statistically significant ($P < 0.05$). The patients of NAFLD had significantly higher levels of triglycerides, total cholesterol, LDL and significantly lower levels of HDL as compared to controls. The difference is statistically significant ($P < 0.05$)

Discussion

NAFLD is a major health burden in developed countries. The prevalence of adult NAFLD in general population of India has been reported between 6.7 - 55.1%.[5] NAFLD is now recognized as a major cause of liver related morbidity and mortality.

NAFLD may progress to liver failure and hepatocellular carcinoma. NAFLD is strongly associated with metabolic syndrome. Insulin resistance and compensatory hyperinsulinaemia have etiologic roles in the development of NAFLD and metabolic syndrome.[6] Chronic inflammation may represent a triggering factor in the origin of the metabolic syndrome and NAFLD: stimuli such as over nutrition, physical inactivity and ageing would result in cytokine hyper secretion and may lead to insulin resistance and diabetes in genetically or metabolically predisposed individuals.

Current data have suggested that two pathogenic pathways are involved in the development and progression of NAFLD: (a) lipotoxicity that induces mitochondrial abnormalities and will increase liver sensitivity to liver inflammatory markers; and (b) enhanced lipid per oxidation by the reactive oxygen species. [7] Two hypotheses have been described in NAFLD. One hypothesis is called the “two-hit model”, being made up of the “first hit” represented by liver steatosis and the “second hit”, which represents the progression of steatosis to steato hepatitis. The other hypothesis is called “multiple parallel hits” and refers to the inter-relationship of insulin resistance, lipotoxicity, oxidative stress, endoplasmic

reticulum stress and gut-micro biota dysfunction. [8, 9]

The chronic low grade inflammation is considered to play a dominant role in the potential development of NASH, hepatic complications (fibrosis, cirrhosis, liver cancer) and extrahepatic complications (cardiovascular diseases, type 2 diabetes mellitus, renal dysfunction). [10]

Findings of our study was in concordance with the study by Foroughi, et al. [11] who found raised levels of serum CRP in NAFLD patients and concluded that rises in circulating CRP levels could be an indicator of the presence of NAFLD and consecutive measurements of CRP can be beneficial in clinical management and follow-up of NAFLD patients. Findings of our study was also in concordance with the study by Abdullah Ozgür Yeniova et al. [12] who revealed that hs-CRP levels were higher in patients of NAFLD as compared to the control group and hs-CRP can be used as a non-invasive marker of NAFLD. Santoshini A et al. [13] and Mansour-Ghanaei, et al.[14] in their research found altered lipid profile (increased triglyceride, total cholesterol, LDL-C and decreased HDL-C) in NAFLD patients. In present study, we found serum total cholesterol, triglycerides, LDL were significantly increased ($p<0.05$) and HDL was significantly decreased ($p< 0.05$) in NAFLD patients as compared to healthy controls.

Conclusion

This case-control study shows that greater elevation of inflammatory marker hs-CRP levels and altered lipid profile in patients of NAFLD as compared to healthy subjects. Inflammatory pathways and alteration in lipid parameters playing pivotal roles in the development and progression of NAFLD & their complications. Further clinical studies with larger sample size are required to address the significance of inflammation in pathogenesis of NAFLD. These pathogenic factors can be used as a prognostic tool for future new therapeutic approach in NAFLD which may facilitate early diagnosis and treatment of non-alcoholic fatty liver and can prevent from long-term complication of fatty liver.

Limitation of the Study

The limitation of this study lies in its relatively small sample size.

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