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A Study of Inflammatory Markers in Patients with Alcoholic-Fatty Liver Disease and Non-Alcoholic Fatty Liver Disease

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ABSTRACT

Background: Increased levels of various circulating chemicals have been associated with fatty liver disease inflammatory markers. The difference in the level of increased inflammatory markers between patients with AFLD and NAFLD is still unclear. **Aims & Objectives:** The aim of the present study was to compare the inflammatory markers between patients with alcoholic-fatty liver disease (AFLD) and non-alcoholic fatty liver disease (NAFLD). mterial and method: This descriptive study included 50 individuals with fatty liver disease (25 NAFLD, 25 AFLD). Venous blood samples were taken from fasting patients to assess inflammatory markers (CRP, IL6, TNF α). Statistical analysis was performed using the student's t- test, with p-values < 0.05 considered significant. **Results:** The mean values of inflammatory markers (CRP, IL6, TNF-α a) in the NAFLD group were 1.79±0.11, 27.94±1.22, 35.24±2.6, and in the AFLD group, 1.92±0.16, 29.35±1.38, 36.88±2.19. There were no significant changes in CRP, IL6, or TNF-α levels between AFLD patients and those with NAFLD. **Conclusion:** Fatty liver disease is associated with increased inflammatory markers. Since increased inflammatory markers in fatty liver disease are indicative of liver injury, due importance should be given to the assessment of inflammatory markers in the management of patients with fatty liver disease.

Key words:
Non-alcoholic fatty liver disease, Alcoholic Fatty Liver Disease, Inflammatory Markers

Introduction

Non-alcoholic fatty liver disease (NAFLD) is a condition closely associated with obesity, type 2 diabetes mellitus (T2DM), hypertension, hyperlipidemia, and metabolic syndrome. NAFLD is a significant cause of end-stage liver disease [1], primary liver cancer, and liver transplantation [2], and is currently the fastest-growing cause of liver-related deaths worldwide [3]. Globally, the prevalence of NAFLD is estimated to be around 25% [4], with up to 80% of obese patients and 47.3–63.7% of patients with T2DM suffering from the condition [5, 6]. As a result, NAFLD poses a significant economic burden on healthcare systems. In order to better understand the factors and mechanisms underlying NAFLD, more comprehensive research is necessary.

NAFLD is widely acknowledged as a hepatic manifestation of metabolic syndrome, with strong linkages to obesity, insulin resistance, increased systemic inflammation, and advanced atherosclerosis. [7] The pathophysiology of NAFLD has not been completely understood. The classic "multiple strikes" theory of NAFLD pathogenesis typically explains the mechanism of progression, which states that lipid accumulation causes hepatic steatosis, which leads to multiple injuries such as adipokine secretion, inflammation, lipotoxicity, and dysregulation of glucose and lipid metabolism, which can eventually lead to non-alcoholic steatohepatitis (NASH) and cirrhosis. [8-10] It is commonly acknowledged that cytokines play an important role as mediators of inflammation, fibrosis, and cirrhosis in NAFLD. [11]

Fatty liver disease (FLD) is one of the leading causes of chronic liver disease around the world. [12] FLD can be caused by excessive alcohol consumption, as in alcoholic fatty liver disease (AFLD), or by non-alcoholic causes, such as non-alcoholic fatty liver disease (NAFLD).The term alcoholic fatty liver disease (AFLD) refers to the initial stage of alcoholic liver disease (ALD), which arises after acute alcohol ingestion and is usually curable with alcohol abstinence. [13-14]. Alcohol and its metabolites can cause inflammation by increasing gut leakiness of microbial products, sensitizing immune cells to stimulus, and activating innate immunological pathways such as the complement system. Ethanol metabolism generates a variety of metabolites, including acetate, reactive oxygen species, acetaldehyde, and epigenetic alterations that can cause inflammatory reactions and illness. [15]

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Previous research has identified various inflammatory mediators involved in the development and progression of NAFLD, including interleukin-1b (IL-1b), interleukin-6 (IL-6), tumor necrosis factor-a (TNF-a), C-reactive protein (CRP), and the NOD-like receptor protein 3 (NLRP3) inflammasome. [16-18] Some of these inflammatory mediators with immunomodulatory properties can be employed as biomarkers to determine the severity and prognosis of NAFLD. [16] Elevated levels of different circulating inflammatory markers have been linked to fatty liver. [19] However, it is unclear whether there is a substantial difference in the degree of elevated inflammatory markers between patients with AFLD and NAFLD. As a result, the current study was conducted to assess the difference in inflammatory markers between AFLD and NAFLD.

Material and Methods:

In this descriptive study, 50 patients diagnosed with fatty liver disease at the Dr. KNS Memorial Institute of Medical Sciences, Gadia, Barabanki, UP, India, between the ages of 30 and 60 were chosen from OPD, clinical, and laboratory visits over a 6-month period.

Sample selection

Patients with a significant history of alcohol consumption exceeding 210 g/week in males and 140 g/week in females for the previous two years, as well as an ultrasound showing fatty liver, were considered to have AFLD, whereas patients with no history of alcohol consumption and an ultrasound showing fatty liver were considered NAFLD. Patients with a history of hepatitis, diabetes mellitus, thyroid diseases, heart illness, or who were taking medicines that affected heart rate variability (HRV) were excluded. The study was carried out with the Ethics Committee's approval, and the goal of the investigation was communicated to all volunteers, who provided informed written consent. In this study, patients were separated into two groups: 25 patients with non-alcoholic fatty liver disease (NAFLD) and 25 patients with alcoholic fatty liver disease (AFLD).

Blood sample analysis

After taking a complete history and following all precautions, 5 ml of venous blood was drawn using a disposable syringe and collected in a sterile clot activator vial. Laboratory tests included inflammatory markers (CRP, IL6, TNF α), and the results were tabulated for statistical analysis.

Statistical Analysis: The statistical analysis was carried out using the SPSS-24 software. The data from the study groups were compared using the Student-t test. The data were reported as mean ± standard deviation, and a p-value < 0.05 indicated statistical significance.

Observation and study

In our study, there were 6 males and 19 females in patients with NAFLD, while in patients with AFLD, only males were present as alcoholic females did not attend OPD due to social stigma/culture as shown in Table no. 1.

Table 1: Comparison of Demographic Profile of All Patients

Variables	NAFLD (Mean ± SD)	AFLD (Mean ± SD)	*P*-value
Age	49.52±8.56	47.54±7.16	0.379
SEX M/F	0:25	6:19	
BMI	26.85±1.76	27.22±1.38	0.165

Table 1 shows the demographic profile of patients with fatty liver disease. There was no significant difference in demographic profile between patients with AFLD and NAFLD.

Graph no.1: Demographic Profile of All Patients

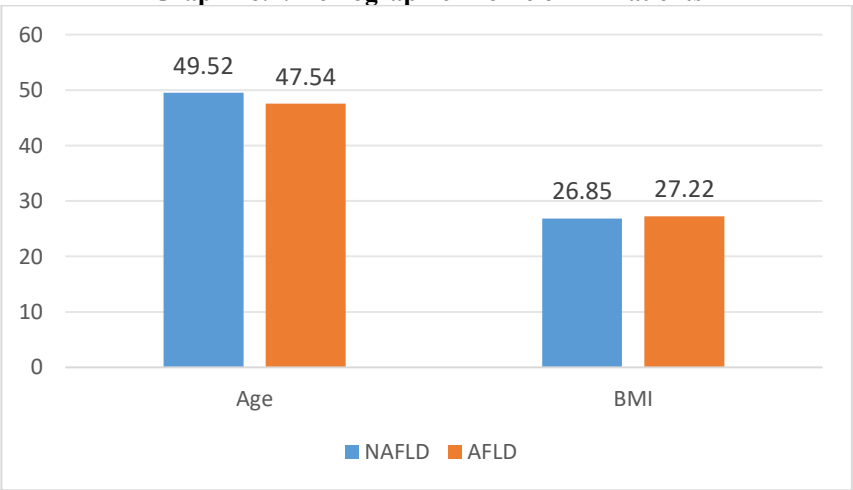
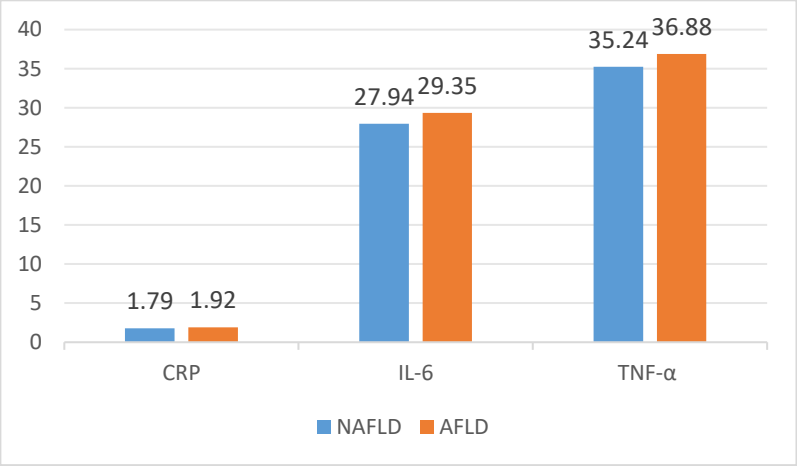


Table No. 2: Comparison of Inflammatory Markers Among NAFLD and FLD Group Patients

Variables	NAFLD (Mean ± SD)	AFLD (Mean ± SD)	*P*-value
CRP mg/dl	1.79±0.11	1.92±0.16	0.002
IL-6 pg/ml	27.94±1.22	29.35±1.38	0.271
TNF-α pg/ml	35.24±2.6	36.88±2.19	0.02

The mean values of inflammatory markers (CRP, IL6, TNF-α a) in the NAFLD group were 1.79±0.11, 27.94±1.22, an 35.24±2.6, whereas and where AFLD group were 1.92±0.16, 29.35±1.38, and 36.88±2.19, as shown in table 2.

Graph no.2: Comparison of Inflammatory Markers Among NAFLD and FLD Group Patients



Discussion

Non-alcoholic Fatty livers have inflammation and liver cell damage, as well as fat in the liver. Inflammation and liver cell damage can cause fibrosis, or steatosis of the liver. Later, it may lead to cirrhosis or liver cancer. Pro-inflammatory cytokines such as TNF-α, IL, interferon, and high-sensitivity C-reactive protein contribute to the pathophysiology of liver disease [20]. Furthermore, excessive lipid buildup in hepatic cells causes oxidative stress by producing an excess of reactive oxygen species (ROS) resulting in hepatic cell lipid peroxidation, cytokine release, and hepatic inflammation [21].

Several studies have been done on fatty liver diseases since its initial description by Ludwig et al. in 1980. Very few studies have been done in India. No comparative descriptive study has yet examined the association of oxidative stress and inflammatory markers in diabetic nonalcoholic fatty liver disease.

Storage of triglycerides in hepatocytes leads to oxidative stress, lipid peroxidation, and pro-inflammatory cytokines such as TNF-α and IL-6. Animal studies suggest that increasing fatty acids in the liver may lead to increased TNF-α levels. When hepatocytes are injured, liver-specific macrophages (Kupffer cells) activate and generate more TNF-α and IL-6 into the bloodstream, leading to the formation of the acute phase protein, high-sensitivity CRP.[22] Several studies have found a link between blood CRP levels and NAFLD. r et al. found that CRP levels were greater in patients with fatty livers, but adiponectin serum levels decreased.[23-26] Targher et al. found that CRP levels were greater in patients with fatty livers, but adiponectin serum levels dserum. ed.[23] Nigma et al. discovered a soutcomes. lly significant link between fatty liver grade and CRP level in serum.[24] Other research showed similar outcomes.[25-26] However, inthe study conducted by Haukeland et al. in Norway, no link between fatty liver grade and CRP le l was found.[27] ;uhowever, found that patients with NAFLD and AFLD had increased levels of inflammatory markers (CRP, TNF-α, IL-6), however this was not statistically significant.

Strengths and Limitations of the Present Study

There are a few limitations of the study. In the present study, only 30-.60-year-old subjects participated in the research. Hence, in the feature, we would like to include an increase in a number of participants to reach a concrete conclusion. The present study was given an impact to understand about the increased concentration of the inflammatory markers involved in the Chronic liver disease.

Conclusion

Inflammatory markers are significantly elevated in both AFLD and NAFLD patients, indicating the presence of low-grade inflammation. Because increased inflammatory markers in fatty liver disease indicate liver injury, assessing inflammatory markers should be prioritized in the therapy of fatty liver disease patients.

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