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A COMPARATIVE STUDY OF INFLAMMATORY MARKERS IN PATIENTS WITH ALCOHOLIC-FATTY LIVER DISEASE AND NON-ALCOHOLIC FATTY LIVER DISEASE

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ABSTRACT

INTRODUCTION: Fatty liver disease is a broad term for the accumulation of triglyceride fat in the liver. Fatty liver disease has been linked to higher levels of different circulating inflammatory markers. The current study compared the inflammatory markers of patients with alcoholic fatty liver disease (AFLD) with non-alcoholic fatty liver disease (NAFLD).

MATERIALS AND METHODS: This descriptive study included 60 individuals with fatty liver disease (30 NAFLD, 30 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 and TNF-α) in the NAFLD group were 01.86±0.57, 27.65±13.58, 34.86±12.34 and in the AFLD group were 01.97±0.74, 29.37±12.19 and 36.12±16.12. There were no significant changes in CRP, IL6, or TNF-α levels between AFLD patients and those with NAFLD.

CONCLUSION: Fatty liver disease is related with elevated inflammatory markers. 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.

Key words: Non-alcoholic fatty liver disease, alcoholic fatty liver disease, inflammatory markers

INTRODUCTION:

Fatty liver disease (FLD) is one of the leading causes of chronic liver disease around the world. [1] 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. [2,3]. 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. [4]

NAFLD is widely acknowledged as a hepatic manifestation of metabolic syndrome, with strong linkages to obesity, insulin resistance, increased systemic inflammation, and advanced atherosclerosis. [5] 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. [6-8] It is commonly acknowledged that cytokines play an important role as mediators of inflammation, fibrosis, and cirrhosis in NAFLD. [9]

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. [10-12] Some of these inflammatory mediators with immunomodulatory properties can be employed as biomarkers to determine the severity and prognosis of NAFLD. [10]

Elevated levels of different circulating inflammatory markers have been linked to fatty liver. [13] 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, 60 patients diagnosed with fatty liver disease at the Warangal hospital and diagnostic center between the ages of 30 and 60 were chosen from OPD, clinical, and laboratory visits over a 6-month period.

Patients with a significant history of alcohol consumption exceeding 210gm/week in males and 140gm/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: 30 patients with non-alcoholic fatty liver disease (NAFLD) and 30 patients with alcoholic fatty liver disease (AFLD).

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-23 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.

RESULTS: In our study, there were 4 males and 26 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 1

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.

Table 1: Demographic profile of all patients

Variables	NAFLD (n=30)	AFLD (n=30)
Age	47.97±6.20	45.91±7.43
SEX M/F	30/0	4/26
BMI	26.17±3.34	26.38±4.32

The mean values of Inflammatory markers (CRP, IL6 and TNF-α) in the NAFLD group were 01.86±0.57, 27.65±13.58, 34.86±12.34 and in the AFLD group were 01.97±0.74, 29.37±12.19 and 36.12±16.12. as shown in table 2

Table 2: Comparison of Inflammatory markers among NAFLD and FLD group patients

Variables	NAFLD (n=30)	AFLD (n=30)	p value
CRP mg/dl	01.86±00.57	01.97±0.74	0.06
IL-6 pg/ml	27.65±13.58	29.37±12.19	0.5
TNF-α pg/ml	34.86±12.34	36.12±16.12	0.08

DISCUSSION:

Pro-inflammatory cytokines such as TNF-α, IL, interferon, and high sensitivity C-reactive protein contribute to the pathophysiology of liver disease [14]. 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 [15].

Storage of triglycerides in hepatocytes leads to oxidative stress, lipid peroxidation, and pro-inflammatory cytokines such 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.[16] Several studies have found a link between blood CRP levels and NAFLD.[17-20] Targher et al. found that CRP levels were greater in patients with fatty livers, but adiponectin serum levels decreased.[17] Nigma et al. discovered a statistically significant link between fatty liver grade and CRP level in serum.[18] Other research showed similar outcomes.[19,20] However, in the study conducted by Haukeland et al. in Norway, no link between fatty liver grade and CRP level was found.[21]

Our study found that patients with NAFLD and AFLD had increased levels of inflammatory markers (CRP, TNF-α, IL-6), however this was not statistically significant.

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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