



## **Association of CRP Levels with Disease Severity in Patients with Alcoholic Liver Disease**

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### **Abstract**

Excessive alcohol intake affects lipid metabolism in the liver, leading to the development of alcoholic liver disease. Detecting appropriate serum biomarkers like c-reactive protein for early and accurate diagnostic methods is vital for the appropriate management of ALD. The published data on C-reactive protein in alcoholic liver disease in India is less. So, the present study was undertaken.

### **Objective**

To estimate the levels of C-reactive protein levels in patients with alcoholic liver disease and its association with the severity of the disease

### **Methods**

This case-control study was done at a tertiary care centre basing on medical records of 100 male

patients. 50 patients were cases, who had alcoholic liver disease and 50 patients were healthy controls.

### **Results**

Most of the patients belonged to the age group 51-60 years. There was a significant difference in the levels of C-reactive protein, parameters of liver function tests and renal function tests, and model for end-stage liver disease score among cases and controls. There was a significant difference in the levels of C-reactive protein levels among cases who varying disease severity.

### **Conclusion**

C-reactive protein test serves as a simple, inexpensive, better alternative to abdomen ultrasound to monitor patients with alcoholic liver disease and its

disease and its progression to cirrhosis of the liver.

### **Keywords**

Alcoholic liver disease, cirrhosis of the liver, hepatitis, C reactive protein, case-control study, disease severity

### **Introduction**

Increased alcohol consumption affects lipid metabolism in the liver, leading to the development of alcohol liver diseases (ALD).<sup>[1,2]</sup> Three types of ALDs include alcoholic fatty liver, alcoholic hepatitis, and alcoholic cirrhosis. Identifying accurate serum biomarkers for AFL is vital for appropriate management. The prevalence of alcoholic liver disease (ALD) is raising globally, especially in India. Previous literature identified that alcohol was the major reason for cirrhosis of the liver (COL).<sup>[3]</sup> Asymptomatic ALD may progress to cirrhosis in around 5–15% of patients in spite of treatment and abstinence and indicated that inflammation along with oxidative stress plays a vital role in the progression to cirrhosis.<sup>[4-5]</sup> C-reactive protein (CRP) is a marker of inflammation, and it is increased in ALD. One meta-analysis proved that the measurement of serum CRP is useful in determining the risk of non-alcoholic steatohepatitis.<sup>[6]</sup> CRP can be useful in predicting the prognosis of alcoholic hepatitis and cirrhosis.<sup>[7-9]</sup>

Alcoholism is responsible for 10.9 to 31% of cases of cirrhosis in India.<sup>[10]</sup> In view of high prevalence of ALD in various parts of India, the current study was designed to study CRP levels and their association with disease severity in patients with ALD.

### **Objective**

To estimate C-reactive protein levels in alcoholic liver disease and its association with disease severity.

### **Materials and Methods**

Study site: Viswabharathi medical college, Kurnool.

Study duration: 6 months from January 2022 to June 2022.

Type of Study: Case-control study conducted in the department of Biochemistry at our medical college.

Sample size: Data of 100 male patients.

These 100 patients were divided into two groups. 50 patients were healthy controls and 50 patients with ALD were cases.

Source of data: We obtained data from the medical records department at our medical college.

### **Inclusion Criteria**

1. Records of male patients aged 18–60 years who were newly diagnosed to have ALD as per ultrasound findings for cases
2. Records of normal patients who had their liver function tests (LFTs) and renal function tests (RFTs), CRP tests done as a part of routine evaluation for controls.

### **Exclusion Criteria**

Records of patients with -

1. History of renal failure, heart disorders, diabetes, and gastrointestinal bleeding in last three months.
2. Viral hepatitis
3. Immunodeficiency.
4. Hepatotoxic drug usage.
5. Smokers

The disease severity was measured using a Model for End-stage Liver Disease (MELD) score. for patient care services.

Parameters Considered -

- Age
- Total bilirubin
- Aspartate aminotransferase (AST)
- Alanine aminotransferase (ALT)

- Alkaline phosphatase (ALP)
- Gamma Glutamyl Transferase (GGT)
- Total protein
- Prothrombin time (PT)
- Serum albumin
- MELD score
- C-reactive protein
- International normalized ratio (INR)
- Serum creatinine

**Statistical Analysis**

Data analysis was done using Epi Info software version 7.2.5. The results were expressed as

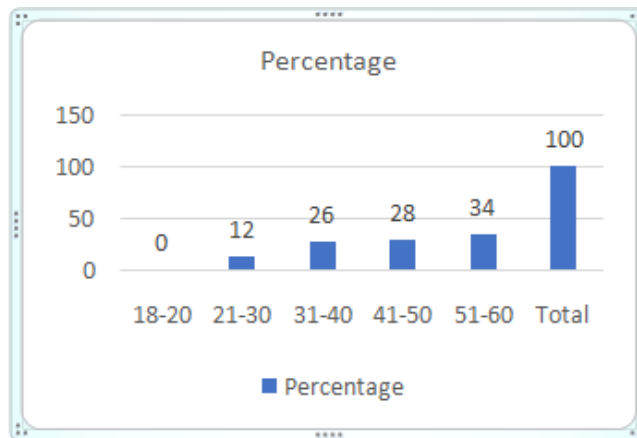
mean  $\pm$  S.D, percentages, and parameters between cases and controls were compared using an independent ‘t’ test. The association between MELD score with CRP levels were assessed among cases by Pearson’s Correlation test’s value  $< 0.05$  was considered as significant.

**Ethical Considerations**

As the study was an observational study, and as the data was taken from medical records, the study underwent an expedited review by the institutional ethics committee and got exempted from taking informed consent from patients.

**Results**

Age: Most of the patients belonged to the 51 to 60 years age group.



**Figure 1:** Age group of patients

There was no significant difference in the mean age between cases and controls (p=0.33).

Mean age	Cases	Controls
	53.7 $\pm$ 2.4	53.2 $\pm$ 2.7 years
T value	0.978	
P value	0.33	

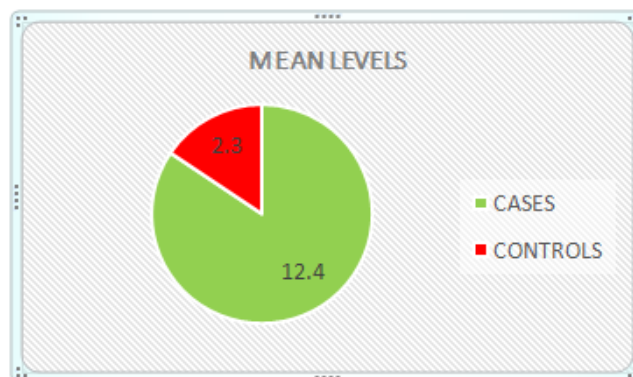
**Table 1:** Mean age of patients in both groups,

**LFT and Serum Creatinine:** There were significant differences in LFTs and serum creatinine between cases and controls, as per T test.

LFT	Cases	Controls	P value
Total Bilirubin (mg/dl)	6.3±1.2	1.1±0.8	<0.01
AST(IU/L)	123±44	24±3.2	<0.01
ALT(IU/L)	62±29	27±6.4	<0.01
ALP(IU/L)	142±23.1	68±13	<0.01
GGT(IU/L)	112±14.3	23±12.4	<0.01
PT(Seconds)	23.1±3.4	12.2±3.1	<0.01
Total protein	5.6±3.1	7.9±1.1	<0.01
Serum albumin	2.7±1.2	4.3±0.64	<0.01
INR	2.04±1.1	1.13±0.41	<0.01
Serum creatinine	1.4±0.8	0.9±0.24	<0.01

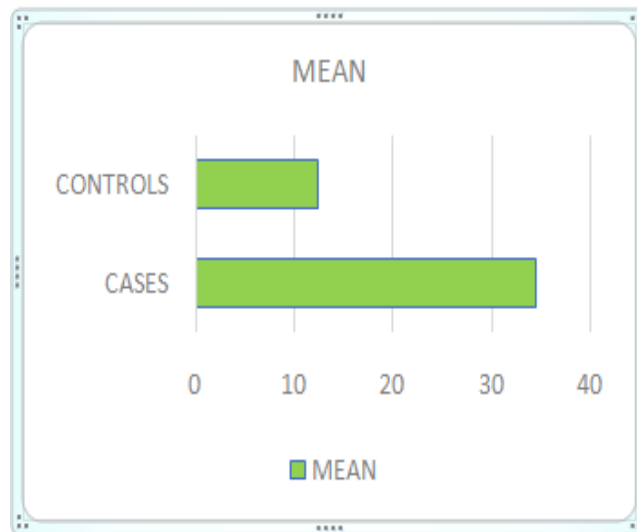
**Table 2:** LFT sand serum creatinine in both groups

CRP: The mean CRP levels in cases were 2.3±0.81 mg/l and it was 12.4±2.1 among controls.



**Figure 2:** Mean CRP levels in both groups

Disease severity- MELD score: Disease severity was assessed by MELD score. The mean MELD score was 34.5±12.3 and 12.8±2.1 among cases and controls. There was a significant difference in the mean MELD score between cases and controls, as per the T-test. (p<0.01)



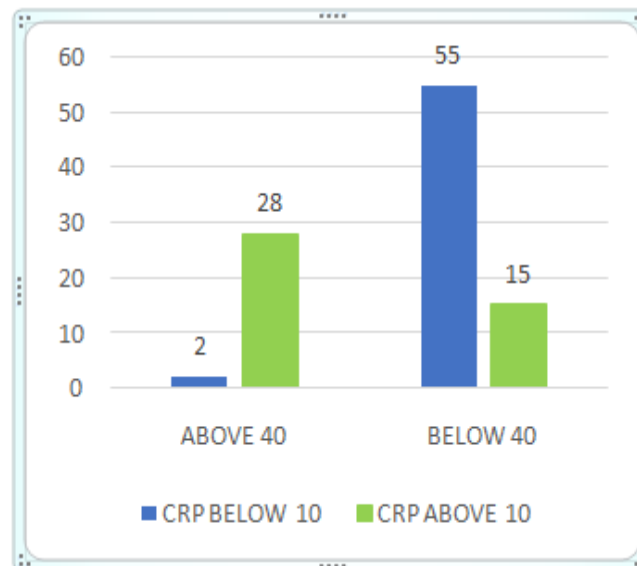
**Figure 3:** Mean MELD scores in both groups

Association between MELD scores and CRP levels:

MELD levels above 50 were seen among 30 patients overall.

CRP above 10mg/l was seen among 43 patients overall.

28 Patients had CRP above 10 mg/l among 30 patients with MELD above 50. There was a significant association between CRP levels and MELD as per chi-square analysis ( $p < 0.01$ ), with a chi-squared value of 44.2. The values as are so taken as normal CRP levels were below 10mg/l and normal MELD levels were below 40.



**Figure 4:** Association between CRP levels and MELD score (disease severity).

### Discussion

The study included 100 patients with 50 cases and 50 controls. Kumara et al. did a study on 30

controls, 30 patients with ALD and found no significant difference between mean age among cases and controls, similar to our study.

Their study showed significant differences in total bilirubin, total protein, serum albumin, AST, ALT, GGT, ALP, hs-CRP between cases and controls, similar to our study.<sup>[11]</sup>

Ciecko et al. found high CRP levels in ALD patients and showed that hs CRP is linked to poor prognosis among these patients.<sup>[12]</sup>In the current study hs-CRP levels were significantly elevated in alcoholic liver disease patients compared to non-alcoholic subjects without any liver disease. These findings were supported by the study of Soulati et al. who showed that CRP can be used as a predictor of mortality among ALD patients.<sup>[13]</sup>The results of this study indicate that inflammation may cause liver injury which in turn raises the severity of the disease which may be linked with various complications related to ALD. Ndumele et al. also found an association between hepatic damage and increased levels of hs-CRP<sup>[14]</sup> Wen Chen et al. found that elevated CRP concentrations at baseline be linked with subsequent increase in the incidence of liver cancer and death from chronic liver disease<sup>[15]</sup>

One study showed that ALT and AST levels along with GGT act as non-invasive markers for liver fibrosis.<sup>[16]</sup> In our study also, we found the same finding. CRP is an acute-phase protein, that is widely studied as a marker of inflammation.<sup>[17]</sup>Apart from cardiovascular disorders, elevated CRP levels were found in patients with liver disease.

The strength of this study was that we included newly diagnosed cases of ALD before any intervention was given and smokers were excluded as smoking can be a confounding factor that affects some of the test parameters. The main limitation is the small sample size. Due to logistic constraints, we didn't take more sample size. Another limitation was that liver

biopsy was not done among cases to detect coexistent hepatitis and cirrhosis, as liver biopsy is an invasive procedure which carries 1% mortality risk.

### **Conclusion**

In the current study, we tested the hypothesis that inflammation (CRP) is associated with disease severity in patients with ALD. The main findings are increased C-reactive protein and LFTs, RFTs among cases compared to controls. C-reactive protein was significantly associated with MELD score in patients with ALD. Alcohol consumption and liver diseases are found to be associated with each other.

As per our study findings, CRP can be used as a non-invasive marker of alcoholic hepatitis among heavy drinkers

The study is self-sponsored.

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