

CRP Levels in Chronic Liver Disease and CRP+CHILD Pugh Score in Liver Disease Patients

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I. Background

Chronic liver disease is a persistent inflammatory state of the liver in which the biochemical and histopathological abnormalities persist over long period. The disease course is featured by a quiescent phase until the development of portal hypertension and deteriorating liver function. The initial quiet phase is called compensated phase of CLD. Development of overt clinical signs like ascites, bleeding manifestations, encephalopathy and jaundice marks the onset of decompensation.

The main objective of prognostic scores in CLD patients is to predict the median survival. However prognostic scores also indicate estimation of hepatic reserve and the capacity to stand up surgery or other aggressive therapeutic interventions. CRP has been evaluated both for the diagnosis of SIRS and for prediction of short term mortality in cirrhosis and addition of these to traditional prognostic scores might improve the prediction of mortality.

The present study was conducted with an aim to study the CRP levels in CLD patients, to evaluate the association between CRP levels and degree of liver dysfunction, to find the utility of CRP used in conjunction with child pugh score in prognosis of CLD

II. Materials And Methods

A cross sectional study was conducted at tertiary care hospital(GOVERNMENT GENERAL HOSPITAL, RANGARAYA MEDICAL COLLEGE, KAKINADA, ANDHRAPRADESH) from February 2018 to July 2019

50 patients of CLD of any etiology greater than 18 years age were included in the study. Patients with hepatocellular carcinoma and other malignancies and autoimmune etiologies and patients who have not given consents were excluded from the study. After obtaining informed consent and ethical clearance patients were subjected to clinical examination and investigated for CBC, LFT, RFT, HbSAG, HCV, USG abdomen, serum electrolytes, serum albumin, PT-INR, CRP, Ascitic fluid analysis, UGI ENDOSCOPY and investigations depending upon the need of the case were performed.

III. Statistical Analysis

All the data obtained are tabulated using Microsoft Excel software. The data is analysed using the statistical package for social sciences (SPSS) software.

The present study included 50 patients with CLD admitted to GGH KAKINADA.

Out of the 50 patients 46 males 4 females

The mean age of presentation is 43.84 with a SD of 10.4 years

Max age of presentation is 68 years and minimum age of years is 23 years

45 patients were alcoholics and 5 were non alcoholics

For 41 patients cause of CLD is alcohol, for 3 patients the cause of CLD is HCV infection, for 1 patient the cause of CLD is HBV, for other 3 patients the cause of CLD is ALCOHOL & HBV infection, for 1 patient the cause of CLD is ALCOHOL & HCV infection

MODE OF PRESENTATION

CLINICAL PRESENTATION	PREVALENCE IN PRESENT STUDY
Abdominal distension	47 (94%)
Jaundice	28 (56%)
Pedal edema	6 (12%)
Altered sensorium	6 (12%)
Pain abdomen	5 (10%)
Reduced urine output	5 (10%)
UGI bleed	4 (8%)
Fever	2 (4%)

MENTAL PRESENTATION

At presentation 36 patients has normal mental status at presentation, 5 had grade 1 HE according to WEST HAVEN grading sytem, 4 had grade 2 HE, 1 had grade 3 HE, 4 had grade 4 HE.

INCIDENCE OF HEMATOLOGICAL ABNORMALITIES

CATEGORY	INCIDENCE
Anemia	92%
Thrombocytopenia	68%
Neutropenia	10%

SERUM BILURUBIN LEVELS AT PRESENTATION

The mean bilirubin at presentation is 7.57 mg/dl, with max value bilirubin being 28.6 mg/dl and the minimum value being 0.3 mg/dl. T he mean bilirubin value among those who survived in study sample was found to be 6.17 mg/dl compared to the higher values among those who did survive that is 12.2 mg/dl and thus it correlated with the outcome with a significant P value of 0.021 (<0.05)

SERUM CREATININE AT PRESENTATION

The mean serum creatinine value at presentation is 1.58 mg/dl, with a max value of serum creatinine being 6.9 mg/dl and min value being 0.5 mg/dl

SERUM ALBUMIN VALUES AT PRESENTATION

The mean value of serum albumin in the present study is 2.50 md/dl, with max value being 4.2 mg/dl and min value being 1.0 mg/dl

SERUM SODIUM VALUE AT PRESENTATION

The mean value of serum sodium in the present study is 130 meq/l , with a max vlue being 146 meq/l and the min value being 120 meq/l

UPPER GI ENDOSCOPY FINDINGS IN THE PRESENT STUDY

CATEGORY	NO.OF PATIENTS
normal	18 (38%)
Portal hypertensive gastropathy	2 (4.8%)
Grade 1 varices	3 (7%)
Grade 2 varices	13 (28.5%)
Grade 3 varices	4 (9.6%)
Grade 4 varices	5 (11.6%)
Pale mucosa	1 (2.1%)

UGI ENDOSCOPY was not done in 3 patients

CRP LEVELS

For comparison purposes, sample data divided into 2 groups wit cutoff value for CRP being set at 10 according to significance noted for CRP in previous studies

CRP LEVELS	FREQUENCY	PERCENTAGE
>=10(group A)	23	46
<10(group B)	27	54
Total	50	100

CORRELATION BETWEEN CRP AND CHILD PUGH SCORE

Patients with CRP levels morethan or equal to 10 had a higher mean value of child pugh score that is 12 with a SD of 1.9 mg/dl when compared to patients with CRP levels less than 10, who had a child pugh score of 9.37 with a SD of1.8 eith significant P value of 0.001

COMPARISON OF RATE OF INFECTIONS WITH REFERENCE TO CRP

In patients wwho had documented evidence of infection tend to have a higher level of CRP that is 18.13 with a SD of 6.2 compared to patients with a mean of 5.6 with SD OF 4.9 in patients who had no such evidence.

COMPARISON OF MORTALITY WITH REFERANCE TO CRP

The mean CRP value in patients who suffered death is 20.43 and a SD of 5.9 compared to a mean of 7.3 and a SD of 6.0 in patients who got survived

CORRELATION BETWEEN CHILD PUGH SCORE AND OUTCOME

Among the study sample of 50 patients, 18 were found to be CLASS B and 32 were found to be in CLASS C. The outcome of the classes of child pugh score is as follows

OUTCOME	CHILD PUGH B	CHILD PUGH C	TOTAL
Death	1	11	12
Survival	17	21	38
Total	18	32	50

The no. Of deaths among 18 pts of CHILD PUGH B were compared with no.of deaths among 32 patients of CHILD PUGH C. The 2 classes were compared using an independent samle T test and the P value of 0.022 was found to be significant

CORRELATION BETWEEN CRP AND CHILD PUGH SCORE

CPS GRADE	N	MEAN CRP	SD
B	18	3.844	4.5894
C	32	13.400	7.4368

COMPARISON OF MELD SCORE WITH CRP AND CHILD PUGH SCORE

OUT COME	N	MEAN MELD SCORE	SD
Death	12	28.08	8.458
Survival	38	19.61	7.123

IV. Discussion

This study was done in a view to note the predictability rate of CRP in conjunction with the Child-Pugh score in the evaluation of patients with chronic liver disease with respect to the assessment of the degree of liver dysfunction and short term prognosis.

The findings noted in the present study are :-

- 1) Patients with chronic liver disease tend to have higher CRP levels with increasing severity of liver disease.
- 2) Infections are the most common cause of mortality in decompensated liver failure patients in the current study.
- 3) CRP is an important parameter in the prediction of infection in patients with chronic liver disease.
- 4) CRP, in conjunction with the Child pugh score, was found to be useful in the prediction of short term mortality of patients with liver disease.

In the present study sample of 50 patients, all the patients with decompensated liver failure were evaluated for the degree of severity of liver disease using Child pugh score and then CRP was measured to further evaluate the short term mortality rate of chronic liver disease.

In the present study, in order to calculate the Child pugh score, each patient has undergone a thorough physical examination to note the presence of ascites and make a note on the mental status of individual and laboratory evaluation to note serum bilirubin, albumin, and PT-INR.

In our study, the mean age of presentation of the patients in the study sample is 43.84, with a standard deviation of 10.4years. The maximum age of presentation in the current sample is 68years, and the minimum age of presentation is 23years. In a study done by Lichen Xu et.al⁷⁸, the mean age was 55.4, in a study done by Jarrier Fernandez et.al⁸⁴, the mean age was 61 and in a study done by Shalimar and Subrat K.Acharya et.al⁷³ it was 45. This may be due to the heavy consumption of illicit alcohol in the population group studied and also due to the commencement of alcohol consumption at an early age

Most common presentation to the hospital in most patients was abdominal distension found in 47 out of 50 patients in the present study followed by jaundice in 28 patients, pedal edema in 6 patients, altered sensorium in 6 patients, abdominal pain in 5 patients reduced urine output in 5 patients, upper gastrointestinal bleed in 4 patients and fever in 2 patients.

In the study done by Shalimar et.al⁷³, all the patients had jaundice followed by abdominal distension in 91.8% cases and altered sensorium in 12.3%.

In the present study 94% had abdominal distension which is of higher value when compared to other studies which may be due to the continued consumption of alcohol despite of the presence of liver disease in the present population and also due to early decompensation observed in the patients of present study . In the present study incidence of upper GI bleed was noted to be 8% compared to 23.9% in the Mukherjee et al . study

In a study done by Mukherjee et.al⁸², uncontrollable ascites was noted in 36.4%, followed by variceal bleeding in 23.9%, and altered sensorium was noted in 13.6% of patients.

In the present study the most common etiological factor was observed to be alcohol.

The number of patients with alcohol addiction is higher when compared to other studies

This can be explained by the fact that patients in this study area are more habituated to alcohol and also addicted to preparations with higher concentrations of alcohol and consume the same in a higher quantity

At presentation in the present study, 36 patients had normal mental status at presentation, 5 patients had grade I hepatic encephalopathy (according to west haven grading of hepatic encephalopathy), 4 had grade II hepatic encephalopathy, 1 had grade III hepatic encephalopathy and 4 had grade IV hepatic encephalopathy.

In the present study patients were followed up for a short course of time compared to other studies, so the real incidence of HE might be higher than what actually represented in the present study

In the present study, the most common hematological abnormality is Anemia, followed by thrombocytopenia and lastly neutropenia.

The mean hemoglobin level in the current study is 8.98, which is higher compared to the study Arisar et al., where it is 8.4 g/dl and lower than that observed in Shalimar et al. study where it is 9.8.

The lower hemoglobin level observed in the present study can be attributed to the coincident finding of iron deficiency anemia in a significant number of patients that would have led to both anemia and relative thrombocytosis observed in some patients

The mean platelet level in the present study is 1,39,000 that is higher than that observed in other studies

The mean bilirubin value at presentation is 7.57 mg/dl, with the maximum value of bilirubin being 28.6 mg/dl and the minimum value being 0.3 mg/dl.

In a study by Malik et al.⁷⁶, the mean serum bilirubin value was found to be 2.28 mg/dl, and in a study done by Arisar et al.⁷⁹, it is 4.33 while in a study done by Shalimar et al.⁷³, the mean serum bilirubin value was found to be 15 mg/dl. The mean values of the current study fall in the median range of the above studies.

The mean bilirubin value among those who survived in the study sample was found to be 6.17 mg/dl compared to the higher values among those who didn't survive that is 12.2 mg/dl, and thus it correlated with the outcome with a significant P value of 0.021 (<0.05).

In the present study, the higher mean serum bilirubin values might reflect the presentation of patients at an advanced stage of the disease and decompensation when compared to other studies.

The mean serum creatinine value at presentation is 1.58 mg/dl, with the maximum value of serum creatinine being 6.9 mg/dl and the minimum value being 0.5 mg/dl.

The serum creatinine values in our study are slightly higher than those observed in previous studies, but this doesn't seem to have an effect on the outcome with a P-value 0.291 (>0.05).

The mean value of serum albumin in the present study is 2.50 mg/dl, with the maximum value being 4.2 mg/dl and the minimum value being 1.0 mg/dl.

The serum albumin values in our study are similar to those seen in C. Arun Kumar et al.⁷⁷ and Shalimar et al.⁷³ but lower than those observed in Malik et al.⁷⁶. The serum albumin values also were not found to be significant. The mean value of serum sodium in the present study is 130 mmol/l, with the maximum value being 146 mmol/l and the minimum value being 120 mmol/l.

The serum sodium values in our study are higher than those seen in C. Arun Kumar et al.⁷⁷ and Shalimar et al.⁷³ but similar to those observed in Malik et al.⁷⁶. The serum sodium values also were not found to be significant. The mean value of PT-INR in the present study is 1.30, with the maximum value being 1.46 and the minimum value being 1.20. The mean PT-INR values in our study are higher than those seen in Lichen Xu et al.⁷⁸ and Arisar et al.⁷⁹ but lower than those observed in Shalimar et al.⁷³. The PT-INR values were positively correlated with the outcome (those having higher values had a higher mortality rate) with a significant P value of 0.001 (<0.005) found to be significant. In a study done by Kim et al.⁸², 36.1% of patients have normal mucosa without varices, 57% have esophageal varices, 25.1% have gastric varices. In the present study sample, 18 patients were found to have Child Pugh grade B, and 32 patients were found to have Child Pugh grade C. The mean Child Pugh score in the present study is 10.58. In a study done by Arisar et al.⁷⁹, 6% of patients were found to have Child-Pugh grade A, 40% of patients were found to have Child Pugh grade B, and 54% of patients have Child Pugh grade C.

Compared to the study done by Arisar et al.⁷⁹, the present study had more number of cases in grade C with none in grade A.

The number of deaths among 18 patients of Child Pugh class B was 1 compared to 11 deaths among the 32 patients of Child Pugh class C. The two classes were compared using an independent sample T-test, and the P value of 0.022 (<0.05) was found to be significant.

In the study done by Arisar et al.⁷⁹, 11 out of 64 patients of class B and 32 out of 77 patients expired with a significant P value of 0.022 (<0.05). This study result is very much comparable to the present study.

In the present study, 18 out of 50 patients had documented evidence of infection. In a similar study done by Arisar et al.⁷⁹, the frequency of infection was found to be 36.66% comparable to the 36% in the present study and the common infections found to be SBP (9%), Gastroenteritis (11%), respiratory and UTI (42%). In patients who had documented evidence of infection tend to have higher levels of CRP that is 18.13 with a standard deviation of 6.2 compared to patients with a mean of 5.6 with a standard deviation of 4.9 in patients

who had no such evidence. Thus CRP at a lower sensitivity level had a good predictability rate for infection with a P value of 0.001(<0.05).

In a study done by Cervoni et.al⁷⁰, found that baseline CRP levels are higher in patients with infection compared to patients without infection.

In a study done by Li CH et.al⁷¹, higher median CRP levels were observed among infected patients. (P<0.001) Lin et.al⁸¹ suggested a lower cut off for CRP in CLD patients with infection to improve the predictability rate for infections.

In patients with Child-Pugh class B, the mean CRP was found to be 3.84 compared to the higher levels in Child-Pugh class C, where it is 13.4mg/dl.

In a study of 148 patients with cirrhosis by mendall et.al⁴⁹, the 6month mortality rate was associated with higher baseline CRP levels.

In the present study, MELD was also calculated as it is currently widely validated as a prognostic indicator in CLD patients. The mean MELD score of the sample study was found to be 21.64, with the maximum score being 40 and the minimum score being 10.

In the present study, the correlation of MELD score with outcome revealed:

- 1) The mean MELD score among the patients not survived is 28.08
- 2) The mean MELD score among the patients survived is 19.61
- 3) The P value is significant that is 0.001(<0.05)
- 4) Comparison of the present study with CRP levels revealed:

The mean MELD score in patients with CRP levels >10 is 23.91, which is comparatively higher compared to 15.23 in those with CRP <10.

V. Conclusions

- 1) The study showed that CRP at a lower sensitivity level can still be useful in the prediction of infection in patients with chronic liver disease.
- 2) CRP also shown to have an effect on the prediction of mortality, since patients with higher levels of CRP, eventually succumbed to death.
- 3) The current study showed a prevalence of infection of about 88% among those who expired during the study period.
- 4) Since CRP is useful in the prediction of infection and prevalence of infection is higher among the patients who expired, the addition of CRP to the traditionally used Child Pugh score can be more useful in the prediction of short term mortality that is proved in the current study.
- 5) The study showed that CRP was useful in the prediction of the severity of liver disease in agreement with both Child Turcotte Pugh score and Model for End Liver Disease (MELD) score. So, CRP can be used as a marker of the severity of liver disease.
- 6) Positive correlation with severity and mortality has also been found with advanced hepatic encephalopathy (grade 3 and 4), serum bilirubin, PT-INR, and MELD score.

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