International Journal of Medicine Research
www.medicinesjournal.com
ISSN: 2455-7404
Received: 26-07-2021, Accepted: 10-08-2021, Published: 26-08-2021
Volume 6, Issue 3, 2021, Page No. 18-21

A comparision of lymphocyte/monocyte ratio with meld and child-pugh scores in patients with liver cirrhosis

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Abstract

Background: To develop an easy and reliable score for evaluating the prognosis of patients with liver cirrhosis has always been challenging**.** LMR is readily available indictor for predicting the prognosis in cirrhosis of liver. This study was undertaken to examine the association of LMR with the MELD and Child Pugh score.

Material and Methods: This study was undertaken in a tertiary care hospital including 30 patients suffering with cirrhosis of liver. Lymphocyte and monocyte counts were obtained from complete blood count results by using standard automated analyzer and LMR was calculated by dividing the lymphocyte count with the monocyte count. Liver failure severity on admission was assessed using the MELD and Child – Pugh scores.

Results: Mean LMR was 2.8, MELD score was 80.13 and CP scores was 11.03 in all the patients in this study. The ROC curve had shown that, LMR had a statistically significant AOC for predicting the prognosis of the disease. The lymphocyte count, serum albumin were higher in the patients with high LMR. Age, monocyte count, serum creatinine, MELD scores and Child Pugh scores were higher in the low LMR group. About 87.5% of the patients with low LMR and 66.7% of the patients with high LMR were categorized as C according to Child Pugh scores.

Conclusion: The LMR can be used as an independent predictor in assessing the prognosis of patients with liver cirrhosis.

Keywords: cirrhosis of liver, Lymphocyte/Monocyte ratio, MELD scores, child pugh score

Introduction

All chronic liver conditions can lead to liver cirrhosis. Liver cirrhosis ultimately results in hepatic decompensation due to portal hypertension, impairment of hepatic biologic functions, or development of cancer [1, 2]. The Global burden of diseases estimates that over a 10 million of deaths occurred in 2010 due to cirrhosis of liver and further a million of deaths due to liver cancer and acute hepatitis. Cirrhosis is late-stage liver disease, in which the liver develops scarring as a result of various long -term challenges. Precipitating causes of cirrhosis include viral hepatitis heavy alcohol consumption,and it is associated with risks for developing primary hepatocellular carcinoma. Advanced cirrhosis is a life threatening condition [3].

Cirrhosis and its complications are a major cause of morbidity and mortality at the community level. Liver has a homeostatic role in the body's immunity and cirrhosis due to any aetiology disrupts the homeostasis [4].

The cell injury and endotoxin release initiated by ethanol and its metabolites also activate innate and adaptive immunity pathways releasing proinflammatory cytokines (eg., TNF-α), chemokines, and proliferation of T and B cells [5].

Bacterial infections are an important cause of morbidity and mortality in patients with liver cirrhosis (LC) due to impaired immune function, together with an increased passage of bacteria from the gut. Monocytes are central mediators of immune response and play a crucial role in the pathogenesis of liver cirrhosis. Inflammatory stimuli mainly affect the numbers of monocytes in the peripheral blood in patients with liver cirrhosis which contributes to Lymphocyte Monocyte Ratio (LMR) changes [6].

Cirrhosis alters the number, subset distribution and function of circulating monocytes. In contrast to the frequently observed leukopenia, cirrhosis is associated with monocytosis B & T lymphocytes are profoundly affected in cirrhosis. There is lymphopenia and is evident since the early stages of cirrhosis [7].

LMR is a readily available and low cost objective marker of systemic inflammation and may be obtained from routine blood testing [8]. In patients with liver cirrhosis, as the disease advances, LMR gets disrupted and decreases compared with MELD and Child Pugh score, which increases with disease progression. Hence this study is undertaken because it is cost effective and easy to calculate and interpret [9]. This study was undertaken in order to determine the role of lymphocyte monocyte ratio in predicting the outcome in patients with liver cirrhosis during their hospital stay and to compare lymphocyte monocyte ratio with MELD and Child Pugh scores.

Material and Methods

This cross sectional study was undertaken in 30 Patients with CLD admitted to hospitals attached to Bangalore Medical College and Research Institute. This study was undertaken for a period of 1.5 Years between November 2018 and May 2020 in hospitals attached to BMCRI. Patients willing to give informed consent, with deranged liver function tests for > 3 months with any of the following features were included in the study group, Ultrasound findings suggestive of chronic liver parenchymal disease, Evidence of decompensated liver cirrhosis with ascites, hepatic encephalopathy, coagulopathy, Previous admissions due to these complications and availability of relevant medical records, Liver biopsy findings suggestive of hepatic fibrosis were included.

Patients aged less than < 18 yrs, those diagnosed with liver cirrhosis, but admitted because of other medical illness, such as diabetes mellitus, ischemic heart disease or cerebrovascular accident, hepatocellular carcinoma, patients with any other concurrent ailment that could alter LMR, such as the presence of hematological malignancy, autoimmune disease or chronic infection like tuberculosis and patients who were administered antibiotics in the last 14 days were excluded from the study.

The patients thus selected were subjected for thorough history and physical examination. Relevant laboratory investigations were ordered including abdominal ultrasonogram and subjected for liver biopsy wherever feasible. Lymphocyte and monocyte counts were obtained from complete blood count results by using standard automated analyzer and LMR was calculated by dividing the lymphocyte count with the monocyte count. Liver failure severity on admission was assessed using the MELD and Child – Pugh scores. MELD was calculated by using standard formula available online and CP score was calculated using five variables (hepatic encephalopathy, INR, ascites, bilirubin and albumin). All the patients were subjected for follow up during their hospital stay. Patients who were successfully managed and discharged from hospital regardless of their duration of hospital stay were included as survived group and those died in the course of treatment due to complications were included as non survived group. The scores were compared between the survivors and non survivors. The data thus obtained was analyzed using Statistical Package for Social Services (IBM Corp: Armonk, NY, USA). Receiver operating characteristic curve was used evaluate the efficacy of the three variables (LMR, MELD & CP score) in determining the outcome in patients with cirrhosis of liver during hospital stay.

Results

Table 1: Comparison of clinical parameters in patients who died and survived

	Survived	Died	Total	P value, Sig
Age in years (Mean ± SD)	44.92 ± 11.9	38.6 ± 1.67	43.87 ± 11.1	0.252, NS
Sex (Male, %)	76.0	100	80.0	0.009, Sig
Lymphocyte count (Mean ± SD)	13.75 ± 7.34	23.3 ± 3.48	15.3 ± 7.7	0.033, Sig
Monocyte count (Mean ± SD)	7.68 ± 3.1	4.3 ± 2.74	7.12 ± 3.26	0.293, NS
Serum creatinine (mg/dl) (Mean ± SD)	1.59 ± 1.5	0.86 ± 0.34	1.47 ± 1.39	0.000, Sig
LMR (Mean ± SD)	1.71 ± 0.9	8.36 ± 6.47	2.8 ± 3.58	0.979, NS
MELD score (Mean ± SD)	81.64 ± 50.2	72.6 ± 45.87	80.13 ± 48.91	0.713, NS
Child Pugh score (Mean ± SD)	10.96 ± 1.48	11.4 ± 1.67	11.03 ± 1.5	0.558, NS

Baseline characteristics

The overall mean age in this study was 43.87 years with mean age of survived patients was 44.92 years and died was 38.6 years. The lymphocyte count and Child Pugh scores were higher in the patients who died when compared with the survived patients. The monocyte count, serum creatinine and MELD scores were higher in patients who survived. A statistically significant difference was seen in Sex, Lymphocyte count and serum creatinine.

Relationship of LMR with MELD and CP scores

Mean LMR was 2.8, MELD score was 80.13 and CP scores was 11.03 in all the patients in this study. Pearson correlation coefficient between the LMR and CP scores was 0.147 and with MELD was -0.127 which was not statistically significant.

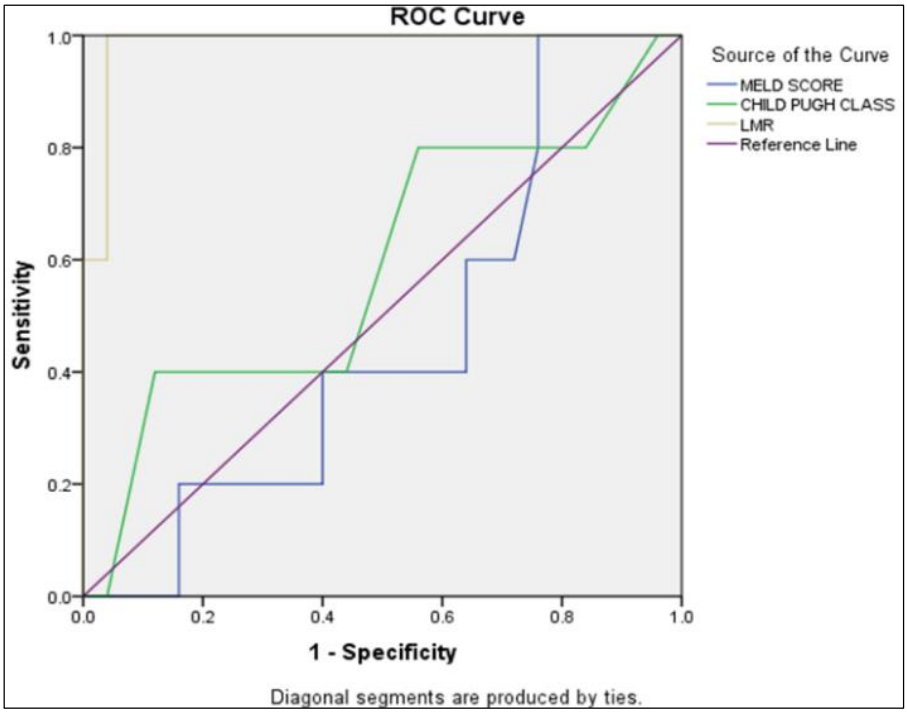

Fig 1: ROC curve showing the AUCs for MELD, CP score and LMR

Table 2: Pair wise comparison of the differences between the areas covered by ROC curve

	Differences between areas	95% CI	P value
CP score – LMR	0.493	0.200 – 0.787	0.959
MELD score – LMR	0.392	0.154 – 0.63	0.422
MELD score – CP scores	0.292	0.105 – 0.524	0.205

ROC curve was used to calculate the AUCs of MELD and CP scores and LMR for determining the outcomes patients with cirrhosis of liver who were survived and died. The ROC curve had shown that, LMR had a statistically significant AOC for predicting the prognosis of the disease. The pair wise comparison of the CP scores – LMR, MELD scores – LMR and MELD scores – CP scores was not statistically significant.

Table 3: Characteristics of variables of the two groups (low vs high LMR)

Characteristics	Low LMR	High LMR	P value, Sig
Age	44.29 ± 11.73	42.17 ± 8.86	0.683, NS
Lymphocyte count	12.95 ± 6.27	24.88 ± 5.05	0.000, Sig
Monocyte count	7.68 ± 3.17	4.9 ± 2.87	0.065, NS
Serum creatinine	1.62 ± 1.52	0.85 ± 0.3	0.231, NS
Serum albumin	2.24 ± 0.53	2.28 ± 0.54	0.857, NS
MELD score	83.42 ± 50.53	67.0 ± 43.26	0.472, NS
Child Pugh score	11.04 ± 1.46	11.0 ± 1.79	0.953, NS

The comparison of clinical parameters used in the study between the patients with low LMR and high LMR scores had shown that, the lymphocyte count, serum albumin were higher in the patients with high LMR. Age, monocyte count, serum creatinine, MELD scores and Child Pugh scores were higher in the low LMR group. Only lymphocyte count was significantly different in low and high LMR group.

Table 4: Association of LMR with Child Pugh class of patients with liver cirrhosis

Child Pugh class	Low LMR N (%)	High LMR N (%)
B	3 (12.5)	2 (33.3)
C	21 (87.5)	4 (66.7)
Total	24 (100)	6 (100)

χ^2 value=1.5 df=1 p value, sig= 0.221, NS

LMR: Lymphocyte Monocyte ratio

This study had shown that, about 87.5% of the patients with low LMR and 66.7% of the patients with high LMR were categorized as C according to Child Pugh scores.

Discussion

The patients with cirrhosis of liver usually demonstrate the systemic inflammation [10]. This inflammation is responsible for the complications associated with the cirrhosis of liver [11]. This study attempted the assessment of the role of inflammatory markers and LMR in the outcome of patients with cirrhosis of liver.

Mean age of survived patients was 44.92 years and died was 38.6 years. The inflammatory markers including lymphocyte count, LMR and Child Pugh scores were higher in deceased patients. A statistically significant difference was seen in Sex, Lymphocyte count and serum creatinine between the patients who died and survived. A study by Jamil *et al* had shown that, the mean age was 53.14 years This study had also shown a significant difference in serum albumin, LMR, MELD scores and CP scores between the patients who were survived and died unlike this study [12]. In a study by Zhang *et al*, most of the patients had decompensated cirrhosis, and significantly low LMR than surviving group [13].

Mean LMR was 2.8, MELD score was 80.13 and CP scores was 11.03 in this study. Pearson correlation coefficient between the LMR and CP scores was 0.147 and with MELD was -0.127 which was not statistically significant. A study by Jamil *et al* had shown that, the mean MELD scores was 11.62, CP score was 9.32 in their study [12]. Zhang *et al* had reported that, LMR was significantly lower in the disease group than the control group [13]. Many studies have shown that, increasing scores predict the worse outcomes in patients with liver cirrhosis [14, 15]. The studies have shown that, LMR can used as an independent predictor of survival in patients with liver cirrhosis [16].

The ROC curve had shown that, LMR had a statistically significant AOC for predicting the prognosis of the disease. The pair wise comparison of the CP scores – LMR, MELD scores – LMR and MELD scores – CP scores was not statistically significant. In a study by Jamil *et al*, the AUC for LMR was 0.807 which was statistically significant. But this study had shown different AUC [12]. A study by Zhang *et al* had shown that, MELD score and LMR were negatively correlated [13].

The lymphocyte count, serum albumin was higher in the patients with high LMR and Age, monocyte count, serum creatinine, MELD scores and Child Pugh scores were higher in the low LMR group where a statistically significant difference was seen with lymphocyte counts. Similar comparison by Jamil *et al* had shown that, MELD scores and Child Pugh scores were statistically significant between the patients with low and High LMR[12].

Conclusion

The LMR can used as independent predictor for prognosis of liver cirrhosis. It can be calculated easily and can be interpreted with efficacy nearly equal to those of MELD and CP scores.

Limitations

This study did not statistically significant correlation between MELD score and Child Pugh score with LMR as we had smaller study population and as more subjects were in CP class C.

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