

Hepatic Artery Resistive Index As A Prognostic Indicator Among Chronic Liver Disease (CLD) Patients In Comparison With Model End-Stage Liver Disease (Meld) Score.

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Abstract:

Background: Contribution of cirrhosis and its complications, collectively chronic liver diseases (C.L.D.s), as causes of mortality in India have been increasing progressively since 1980. The cultural–lifestyle transition India is currently passing through with the progressive adoption of a western diet, sedentary habits, and an aura of freedom from long-held taboos around alcohol in the society create grounds for a spectrum of liver diseases in India. The diagnosis and therapeutic management of patients with chronic liver disease depend on an accurate assessment of the level of hepatic fibrosis. For more than 20 years, Doppler ultrasonography (US) has been used to evaluate arterial blood flow in people with liver cirrhosis.

To prioritize patients for organ transplants based on severity and three-month survival rates, the United Network for Organ Sharing first adopted the MELD score in 2002. Later, it was used by numerous hospitals and nations to rate transplant candidates and evaluate survivability, respectively.

This study aims to investigate the link between hepatic arterial hemodynamic characteristics and the Model End-Stage Liver Disease (MELD) score. A commonly used standardized scoring system can be related to the parameters, which are assessed using ultrasonography Doppler to assess the patient's severity and likelihood of survival.

Materials and Methods: In this cross-sectional study, 30 patients coming to the department of radiodiagnosis for abdominal ultrasound and were clinically diagnosed with Chronic Liver Diseases (CLD) at Hanagal Shri Kumareshwara hospital, Bagalkot.

Results: The correlation between resistive index and MELD score was statistically significant with correlation co-efficient of 0.735 and p-value of <0.001.

Conclusion: The death rate from chronic liver disease has increased significantly in recent years. A practical, non-invasive alternative that offers precise information on chronic liver disease is colour Doppler sonography. In individuals with chronic liver disease, we saw a substantial correlation between the MELD score and the hepatic artery RI value. The current results further suggest that Doppler US can offer helpful information for determining the prognosis in individuals with chronic liver disease.

Key Word: Chronic liver disease (CLD), Colour Doppler sonography, Hepatic artery doppler, MELD score, Model End-Stage Liver Disease (MELD) score.

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I. Introduction

Any disorder that causes persistent or recurring hepatocyte death and hepatic cirrhosis are referred to as chronic liver disease. Alcohol usage and viral hepatitis are the two most frequent causes. Cirrhosis can also be caused by chronic biliary injury or obstruction, which can happen in primary biliary cirrhosis, sclerosing cholangitis, and post-surgical biliary strictures. Other causes of CLD include Alpha-1-antitrypsin deficient Wilson's disease, Cystic Fibrosis, Autoimmune Liver Disease, Haemochromatosis, Non-alcoholic Fatty Liver Disease (NAFLD), and Cystic Fibrosis.¹

The diagnosis and therapeutic management of patients with chronic liver disease depend on an accurate assessment of the level of hepatic fibrosis. For more than 20 years, Doppler ultrasonography (US) has been used to evaluate arterial blood flow in people with liver cirrhosis. Liver span, shape echotexture, surface irregularity, nodularity portal vein measurement, and portal vein doppler are only a few of the parameters that are determined throughout the process.²⁻⁴

The arterial resistance index (RI) is the doppler US measure most frequently employed in clinical investigations to calculate intrahepatic vascular resistance. Liver fibrosis relates to a hepatic artery RI >0.70.⁵⁻⁸

To predict survival in patients with cirrhosis of the liver scheduled for transjugular intrahepatic portosystemic shunt, the Model for End-Stage Liver Disease (MELD) score was created in 2000 (TIPS).² The distribution of donated livers for transplant is decided using the MELD grading method, which was created to predict short-term mortality in patients with liver cirrhosis.^{3,9,10} Serum bilirubin, serum creatinine, and the international normalized ratio of prothrombin time (INR) are three straightforwardly measurable objective biochemical markers that form the basis of the MELD score. In patients with cirrhosis who are listed for orthotopic liver transplantation, the MELD score is a highly accurate predictor of 3-month mortality.^{9,10} An increasing MELD score is linked to worsening hepatic dysfunction and a higher chance of dying within three months in cirrhotic patients.

To prioritize patients for organ transplants based on severity and three-month survival rates, the United Network for Organ Sharing first adopted the MELD score in 2002. Later, it was used by numerous hospitals and nations to rate transplant candidates and evaluate survivability, respectively.^{9,12}

This study aims to investigate the link between hepatic arterial hemodynamic characteristics and the Model End-Stage Liver Disease (MELD) score. A commonly used standardized scoring system can be related to the parameters, which are assessed using ultrasonography Doppler to assess the patient's severity and likelihood of survival.

II. Material And Methods

The material for the present study is patients coming to the department of radiodiagnosis for abdominal ultrasound and clinically diagnosed with Chronic Liver Diseases (CLD) at Hanagal Shri Kumareshwara hospital, Bagalkot.

Study Design: Cross sectional study

Study Location: This was a tertiary care teaching hospital-based study done in Department of Radiodiagnosis, at S Nijalingappa Medical College and HSK Hospital, Bagalkot, Karnataka, India.

Study Duration: February 2021-April 2022

Sample size: 30 patients.

Sample size calculation: Sample size estimation was done using Medcalc software.

At 95% confidence level, and 95% power of the study α (two-tailed) = 0.050 and at 95% confidence level.

$B = 0.200$ and 80% of power of the study. The standard normal deviate for $\alpha = Z\alpha = 1.960$

The standard normal deviate for $\beta = Z\beta = 0.842$. Sample size estimated is 26, which is taken as 30.

Formula used: $N = \frac{([Z\alpha + Z\beta]/C)^2}{p(1-p)}$, where $C = 0.5 * \log_e\left(\frac{1+r}{1-r}\right)$

Subjects & selection method: The material for the present study is from patients coming to the department of Radiodiagnosis for abdominal ultrasound and clinically diagnosed with Chronic Liver Diseases (CLD) at S Nijalingappa Medical College and HSK Hospital, Bagalkot. To meet the objectives of our study, a primary source of information technique was adopted with direct interview method using pre-tested semi-structured questionnaire and by doing abdominal ultrasound and doppler ultrasound of the hepatic artery by standard methods.

Inclusion criteria:

1. All patients diagnosed with chronic liver disease and are reporting for abdominal ultrasound.
2. Patients who have given written informed consent.

Exclusion criteria:

1. Patients with renal diseases.
2. Patients undergoing dialysis.
3. Patients with cardiac illness.
4. Patients diagnosed with carcinoma.
5. Patients diagnosed with bleeding disorders.
6. Patients of RTA/Hepatic injury patients.

Procedure methodology

After written informed consent was obtained, a well-designed questionnaire was used to collect the data of the recruited patients retrospectively. The questionnaire included socio-demographic characteristics such as age, gender, nationality, lifestyle habits like smoking and alcohol, and clinical and biochemistry laboratory investigations such as Serum bilirubin, Serum creatinine & PT INR.

All patients will undergo ultrasonography of abdomen, using a curvilinear probe of 2 – 5Mhz, coupled with color Doppler equipment. The patient was asked to lie supine in a comfortable position while the USG was performed. Doppler waveforms were recorded for at least five seconds in suspended expiration (end expiratory).

Doppler studies were performed after overnight fasting. Doppler study was performed with Duplex Doppler apparatus with color Doppler sonographer and 3.75 MHz convex transducer is chosen for assessment of deep vessels. The Hepatic artery and portal veins best interrogated by Doppler ultrasound of porta hepatis using oblique intercostal scans. Parameters such as Hepatic artery Peak systolic velocity and Peak diastolic velocity calculated. Using these parameters Hepatic artery Resistive index (HARI) is calculated as follows:

Hepatic artery Resistive index (RI) = (Peak systolic velocity - Peak diastolic velocity)/Peak systolic velocity.

Model for End-Stage Liver Disease (MELD) score is a prognostic scoring system, based on laboratory parameters, used to predict 3-month mortality due to liver disease. MELD score was calculated in all patients of our study. MELD score uses the patient's values for serum bilirubin, serum creatinine, and the international normalized ratio for prothrombin time (INR) to predict survival. It is calculated according to the following formula.

$$0.957 \cdot \log(\text{creatinine mg/dl}) + 0.378 \cdot \log(\text{total bilirubin [mg/dl]}) + 1.120 \cdot \log(\text{INR}) + 0.643.$$

MELD scores range from 6 to 40; the higher the score, the higher the 3-month mortality related to liver disease. In interpreting the MELD score in hospitalized patients, the 3-month mortality is:

MELD score	Mortality at 3 months
40 or >	71.3% mortality
30 – 39	52.6% mortality
20 – 29	19.6% mortality
10 – 19	6% mortality
< 9	1.9% mortality

Statistical analysis

Data was entered in an excel sheet and analyzed using the Statistical Package for the Social Sciences 19 (SPSS Inc. Chicago). Results were presented in tabular and graphical forms Mean, median, standard deviation and ranges were calculated for quantitative data. The Chi square test was applied for proportions. Later appropriate tests of significance were applied. P<0.05 were considered as statistically significant.

III. Result

The correlation between resistive index and MELD score was statistically significant with correlation coefficient of 0.735 and p-value of <0.001. The correlation between PSV and MELD score was statistically significant with correlation co-efficient of 0.452 and p-value of 0.012.

Table no 1 shows our study's etiology of chronic liver disease. We found that most of the patients were alcoholic (50%), which was the cause of chronic liver disease, followed by hepatitis (33.3%)

Table no 1: Distribution of the etiology of chronic liver disease.

Etiology	Frequency	Percentage
Hepatitis	10	33.3%
Alcohol	15	50%
Non-alcoholic fatty liver disease	3	10%
Autoimmune liver disease	1	3.3%
Wilson's disease	1	3.3%
Total	30	100%

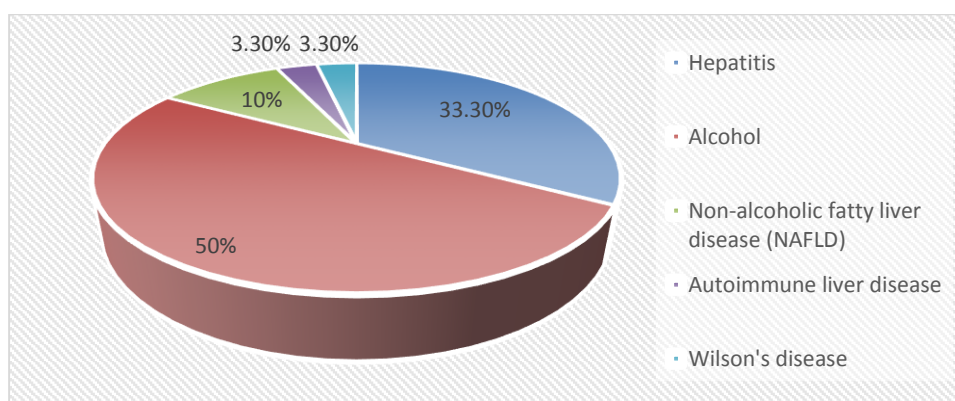


Table no 2: Shows the mean values of biochemical parameters like serum bilirubin, serum creatinine, and INR. The mean serum bilirubin was 4.7 ± 3.54 mg/dl, our study's mean serum creatinine levels were 1.7 ± 0.82 mg/dl, and the mean INR was 1.59 ± 0.71 . The mean values of resistive index (RI) and MELD score. The mean resistive index was 0.77 ± 0.13 , The mean MELD score was 20.52, with a SD of 7.06

Table no2: Mean values of biochemical & other parameters

Biochemical parameters	Mean \pm SD
Serum bilirubin (mg/dl)	4.7 \pm 3.54
Serum creatinine (mg/dl)	1.7 \pm 0.82
INR	1.59 \pm 0.71
Hepatic artery RI	0.77 \pm 0.13
MELD Score	20.52 \pm 7.06

Table no3: Shows there was a statistically significant correlation with biochemical parameters like serum bilirubin and serum creatinine ($p < 0.05$). We found a significant positive correlation between MELD score and doppler parameters like resistive index ($p < 0.05$).

Table no 3: Correlation of MELD score with biochemical, USG, and doppler parameters.

MELD score	Correlation coefficient	p-value
Serum bilirubin	0.4085	0.025
Serum creatinine	0.7364	<0.001
INR	0.637	<0.001
Liver size	-0.5292	0.003
Resistive index	0.735	<0.001

IV. Discussion

The diagnosis and therapeutic management of patients with chronic liver disease depend on an accurate assessment of the degree of hepatic fibrosis. Despite being the gold standard for cirrhosis and fibrosis diagnosis and grading, a percutaneous biopsy is an intrusive procedure and cannot be utilized for follow-up. Furthermore, 20% to 30% of patients experience erroneous negative results from histological analysis of liver biopsy tissues due to improper collection.¹⁴ Because of this, non-invasive techniques for identifying liver fibrosis and cirrhosis are increasingly important.

Measurement of the relative flow or velocity in the hepatic artery or vein and in the portal vein has been the focus of such research because Doppler US enables quantitative blood flow measurement to the liver. As a result, many researchers have investigated the utility of Doppler US as a non-invasive method of determining the degree of hepatic fibrosis.^{3-8,14,15.}

Hence the present study was planned to determine the relationship between Model End-Stage Liver Disease (MELD) score and hepatic arterial hemodynamic parameters, Resistive index (RI) measured via ultrasound Doppler.

According to this study, hepatitis virus infection (33.3%) and heavy alcohol intake (50%) were the main risk factors for CLD. These results were close to those of research conducted in Lagos, Nigeria, by Lesi et al.¹⁶, in which 58% of CLD patients tested positive for hepatitis B, and 12% tested positive for hepatitis C. The study by Nwokediuko et al.¹⁷ in Enugu, Nigeria, in which 49.4% of CLD patients tested positive for hepatitis B and 8.4% for hepatitis C, also had findings similar to this one. However, 74.3% of the participants in a different study by Nwokediuko et al.¹⁸ was positive for hepatitis B. The most significant causes of chronic liver disease, such as liver cirrhosis and liver cancer, which ultimately lead to early death, have been identified as hepatitis B virus and hepatitis C virus.¹⁹

According to Ohnishi et al. and Sacerdoti et al. investigations, portal and splanchnic circulation alterations are a hallmark of liver cirrhosis.^{5,20-22} Splanchnic vasodilation is linked to increased portal venous blood flow resistance. Doppler ultrasonography has been used as a non-invasive approach to assess renal and portal hemodynamics. Cirrhotics have been observed to have poor portal vein flow.

Hepatic artery RI values were found to be elevated in earlier research on individuals with chronic liver disease, which was assumed to be connected to the structural alterations in the liver that occur as the disease severity increases.^{7,8} According to a recent study by Piscaglia et al.⁷, a rise in the RI value is associated with an increase in the histologic fibrosis score. However, necrosis or inflammation was not associated with the overall histologic score. The RI value is typically influenced by various factors, such as patient age and heart rate, and most studies have found no association between the RI value and histological findings.³

The MELD scoring system was created to address the shortcomings of the Child-Pugh rating in patients with end-stage liver disease. It has been proven that the MELD score estimates 3-month survival more correctly than the Child-Pugh score.²³

There is only one study in the literature that examined individuals with chronic liver disease and compared the MELD score and etiological variables. Angermayr et al.²⁴ found no statistically significant difference between the groups in the 3-month period when they evaluated the etiology-based MELD score and survival in patients with alcohol- and viral-induced cirrhosis. However, during a 12-month period, patients with viral hepatitis-induced cirrhosis had MELD scores that were considerably higher and a worse survival rate. They provided the following explanation for their findings: liver disease advances in people with untreated viral hepatitis and in people who are not responsive to treatment, but it does not advance in people with alcohol-induced cirrhosis because these people stop drinking after receiving a diagnosis.

As a result, unlike individuals with hepatic cirrhosis, patients with alcohol-induced cirrhosis do not have a significant increase in the MELD score over time. The MELD score and the etiological variables for liver cirrhosis were not significantly correlated in the current investigation; however, the MELD score was only calculated once when Doppler US was conducted.

The MELD score and the hepatic artery RI are strongly associated with the current report. In a study by Westra et al.²⁵ including 38 kids with end-stage liver disease, it was discovered that the hepatic artery RI value had significantly increased. Additionally, it was noted by Iwao et al.²⁶, Sacerdoti et al.⁵, and Westra et al.²⁵ that cirrhosis patients had considerably higher hepatic artery RI and PI values.

In a comparable study, Yan et al.¹²⁷ examined the MELD score and the extent of liver fibrosis in 53 patients with liver cirrhosis and found a correlation between the two measures. The individuals in the current study who scored the highest for MELD also had the highest hepatic artery RI values.

Iwao et al.²⁶ reported that cirrhotic patients' hepatic artery buffer capacity was considerably lower than healthy controls. Despite compensatory alterations in portal venous flow, the portal vein cannot make up for variations in flow and pressure that occur in the hepatic artery. Additionally, because the portal vein is made up entirely of extrahepatic splanchnic blood flow, it cannot regulate its flow. As a result, changes in portal vascular flow or resistance cannot make up for changes in hepatic artery perfusion.

Sacerdoti et al.⁵ observed that the hepatic artery PI value is higher in cirrhotic patients than in healthy individuals, which is consistent with our findings. Iwao et al.²⁶ reported that patients with cirrhosis and portal hypertension (PHT) had higher hepatic artery PI values than healthy controls.

More and more studies are using the MELD score system to evaluate the prognosis of hepatic parenchymal disorders. The MELD score is typically selected over alternative scoring systems because it is an objective indicator based on accepted laboratory data that can precisely determine prognosis.

V. Conclusion

The death rate from chronic liver disease has increased significantly in recent years. A practical, non-invasive alternative that offers precise information on the location and kind of chronic liver disease is color Doppler sonography. In individuals with chronic liver disease, we saw a substantial correlation between the MELD score and the hepatic artery RI value. The current results further suggest that Doppler US can offer helpful information for determining the prognosis in individuals with chronic liver disease.

References

- [1]. Innes JA. Davidson's essentials of medicine. 2nd ed. London, England: Churchill Livingstone; 2015.
- [2]. Lim AKP, Patel N, Eckersley RJ, Kuo Y-T, Goldin RD, Thomas HC, et al. Can Doppler sonography grade the severity of hepatitis C-related liver disease? *AJR Am J Roentgenol.* 2005;184(6):1848–53.
- [3]. Glišić TM, Perišić MD, Dimitrijević S, Jurišić V. Doppler assessment of splanchnic arterial flow in patients with liver cirrhosis: correlation with ammonia plasma levels and MELD score: Splanchnic Arteries in Cirrhotic Patients. *J Clin Ultrasound.* 2014;42(5):264–9.
- [4]. Haktanir A, Cihan BS, Celenk C, Cihan S. Value of Doppler sonography in assessing the progression of chronic viral hepatitis and in the diagnosis and grading of cirrhosis. *J Ultrasound Med.* 2005;24(3):311–21.
- [5]. Sacerdoti D, Merkel C, Bolognesi M, Amodio P, Angeli P, Gatta A. Hepatic arterial resistance in cirrhosis with and without portal vein thrombosis: relationships with portal hemodynamics. *Gastroenterology.* 1995;108(4):1152–8.
- [6]. Colli A, Cocciolo M, Mumoli N, Cattalini N, Fraquelli M, Conte D. Hepatic artery resistance in alcoholic liver disease. *Hepatology.* 1998;28(5):1182–6.
- [7]. Piscaglia F, Gaiani S, Calderoni D, Donati G, Celli N, Gramantieri L, et al. Influence of liver fibrosis on hepatic artery Doppler resistance index in chronic hepatitis of viral origin. *Scand J Gastroenterol.* 2001;36(6):647–52.
- [8]. Liu C-H, Lin J-W, Tsai F-C, Yang P-M, Lai M-Y, Chen J-H, et al. Noninvasive tests for the prediction of significant hepatic fibrosis in hepatitis C virus carriers with persistently normal alanine aminotransferases. *Liver Int.* 2006;26(9):1087–94.
- [9]. Chung IS, Park M, Ko JS, Gwak MS, Kim GS, Lee S-K. Which score system can best predict recipient outcomes after living donor liver transplantation? *Transplant Proc.* 2012;44(2):393–5.
- [10]. Suzuki H, Bartlett ASR, Muiesan P, Jassem W, Rela M, Heaton N. High model for end-stage liver disease score as a predictor of survival during long-term follow-up after liver transplantation. *Transplant Proc.* 2012;44(2):384–8.
- [11]. Gleisner AL, Muñoz A, Brandao A, Marroni C, Zanotelli ML, Cantisani GG, et al. Survival benefit of liver transplantation and the effect of underlying liver disease. *Surgery.* 2010;147(3):392–404.
- [12]. Merion RM, Schaubel DE, Dykstra DM, Freeman RB, Port FK, Wolfe RA. The survival benefit of liver transplantation. *Am J Transplant.* 2005;5(2):307–13.

- [13]. SHEN L, LI JQ, ZENG MD, LU LG, FAN ST, BAO H. Correlation between ultra-sonographic and pathologic diagnosis of liver fibrosis due to chronic virus hepa-titis. *World J Gastroenterol* 2006; 12: 1292-1295.
- [14]. Lim AK, Patel N, Eckersley RJ, et al. Can Doppler sonography grade the severity of hepatitis C-related liver disease? *AJR Am J Roentgenol* 2005;184(6): 1848–1853.
- [15]. Popov D, Krasteva R, Ivanova R, Mateva L, Krastev Z. Doppler parameters of hepatic and renal hemodynamics in patients with liver cirrhosis. *Int J Nephrol* 2012: 961654.
- [16]. Lesi OA, Kehinde MO, Anomneze EE. Chronic liver disease in Lagos: a clinicopathological study. *The Nigerian Postgraduate Medical Journal* 2004; 11(2): 91-96.
- [17]. Nwokediuko SC, Osuala PC, Uduma UU, Alaneme AK, Onwuka CC, Mesigo C, et al. Pattern of liver disease admissions in a Nigerian tertiary hospital. *Niger J ClinPract* 2013; 16: 339-342.
- [18]. Nwokediuko SC, Ibegbulam OG. Quantitative platelet abnormalities in patients with Hepatitis B virus-related liver disease. *Gastroenterology Research* 2009; 2(6): 344-349
- [19]. Naveau S, Perlemuter G, Balian A. Epidemiology and natural history of cirrhosis. *Rev Prat* 2005; 55: 1527-1532
- [20]. Ralls PW. Color Doppler sonography of the hepatic artery and portal venous system. *AJRAm J Roentgenol*. 1990 Sep;155(3):517-25.
- [21]. Vassiliades VG, Ostrow TD, Chezmar JL, Hertzler GL, Nelson RC. Hepatic arterial resistive indices: correlation with the severity of cirrhosis. *Abdom Imaging* 1993;18(1):61–65.
- [22]. Sacerdoti D, Bolognesi M, Markel C, Angeli P, Gatta A. Renal vasoconstriction in cirrhosis evaluated by Duplex Doppler Ultrasonography. *Hepatology* 193:17:219-24.
- [23]. A Model to Predict Survival in Patients with End-Stage Liver Disease Patrick Kamath S.H. Wiesner, Michael Malinchoc (*HEPATOLOGY* 2001; 33: 464-470.
- [24]. Angermayr B, Luca A, König F, Bertolini G, Ploner M, Gridelli B, Ulbrich G, Reiberger T, Bosch J, Peckradosavljevic M. Aetiology of cirrhosis of the liver has an impact on survival predicted by the model of end-stage liver disease score. *Eur J Clin Invest* 2009; 39: 65-71.
- [25]. Westra Sj, Zaninovic Ac, Vargas J, Hall Tr, Boechat Mi, Busuttill Rw. The value of portal vein pulsatility on duplex sonograms as a sign of portal hypertension in children with liver disease. *Am J Roentgenol* 1995; 165: 167-72.
- [26]. Iwao T, Toyonaga A, Oho K, Tayama C, Masumoto H, Sakai T, Sato M, Tani-Kawa K. Value of Doppler ultrasound parameters of portal vein and hepatic artery in the diagnosis of cirrhosis and portal hypertension. *Am J Gastroenterol* 1997; 92: 1012- 1017.

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