Original Research Article

Evaluation of abnormal hematological indices in liver cirrhosis

Viji Devanand, Anto Nazarene F, Niveditha P, Sathishkumar S

Department of Physiology, Stanley Medical College, Chennai, Affiliated to the Tamil Nadu Dr. MGR Medical University, Chennai, Tamil Nadu, India

Abstract

Background: Cirrhosis of liver is characterised by irreversible scarring and fibrosis leading to long term damage of the hepatocytes. The etio-pathogenesis of the hematological abnormalities in cirrhosis is multi-factorial and is associated with increased risk of complications. A**im:** To evaluate the abnormalities in various hematological indices in patients with cirrhosis of various etiologies and correlate them with the Model for End stage Liver Disease (MELD) score in patients with cirrhosis. **Materials and Methods:** It was a descriptive cross-sectional study of 60 patients with liver cirrhosis. The hematological indices such as hemoglobin, RBC count, PCV, WBC count, DC, platelet count, MCV, MCH, MCHC and RDW were evaluated. The MELD (Model for End stage Liver Disease) score was calculated and correlated with the abnormalities in the hematological indices using Pearson's Correlation coefficient. **Results:** Among the study population, 53 (88.33%) were males and 7 (11.67%) were females. Alcohol induced decompensation was the commonest cause (63.33%) of cirrhosis followed by Hepatitis B (6.67%). The abnormalities in hematological indices were identified. The mean value of the MELD scores of the study population was 17.11 ± 8.4. There was no significant correlation between the hematological indices and the MELD scores. **Conclusion:** Although abnormalities in hematological indices were identified in the patients with cirrhosis, there was no correlation with the MELD scores. Further studies with larger samples are planned as it could be of some help in preventing complications and could contribute to better prognosis.

Keywords: cirrhosis, hematological indices, liver

Corresponding author
Dr. Anto Nazarene F, Postgraduate Student, Department of Physiology, Stanley Medical College, 305 OSH Road, Royapuram, Chennai, Tamil Nadu 600001
Telephone: + 91 9789364015, Email: drantonazarene@gmail.com

Introduction

Cirrhosis of liver is characterised by irreversible scarring and fibrosis leading to long term damage of the hepatocytes.[1] The commonest causes of cirrhosis are alcoholic hepatitis and viral hepatitis (B and C).[2] The other causes include Non-alcoholic steatohepatitis (NASH), primary biliary cholangitis, autoimmune hepatitis, primary sclerosing cholangitis, hereditary hemochromatosis, Wilson's disease, glycogen storage disorders, cardiac cirrhosis, hepatotoxic drugs or toxins, alpha1- antitrypsin deficiency and cystic fibrosis.[1,2]

Cirrhosis is often preceded by hepatitis and fatty change or steatosis. As a result of cirrhotic changes, the fibrous tissue bands replace the entire liver architecture leading to reduced blood flow. The spleen becomes congested which leads to hypersplenism.[3] Portal hypertension is the reason behind most of the severe complications of cirrhosis.[4]

Cirrhosis of liver is one of the risk factors for hepatocellular carcinoma.[5]

According to the World Health Organisation (WHO) report, liver cirrhosis is the 14th leading cause of deaths worldwide and could be the 12th leading cause of deaths worldwide by 2020. Liver disorders are the tenth most common cause of death in India and about 10 lakh new patients are diagnosed with cirrhosis every year in India. Cirrhosis is associated with various hematological abnormalities which are multi-factorial in origin. We need lot of research to be done in liver cirrhosis, its etio-pathogenesis, prognosis and clinical outcomes considering the epidemiological variations in our country. We were therefore interested in the topic. The objectives of this study were to evaluate the abnormalities in various hematological indices in patients with cirrhosis of various etiologies and to correlate the abnormal hematological indices with Model for End stage Liver Disease (MELD) score in patients with cirrhosis

Materials and Methods

A cross sectional study was done among 60 patients with liver cirrhosis of various etiologies. The study participants were selected from the Medical Gastro-enterology (MGE) OPD and MGE wards of Stanley Medical College Hospital, Chennai. The study was done between July 2018 and September 2018. The following were the inclusion and exclusion criteria:

Inclusion criteria: Patients who have been diagnosed with liver cirrhosis (of various etiologies), both males and females, age > 12 years.

Exclusion criteria: Unconscious and Coma patients, patients with primary hematological disorders, patients on chemotherapy or radiotherapy and bone marrow suppressing agents, any other chronic or end stage diseases.

Data collection was done after obtaining clearance from the Institutional Ethics Committee. After obtaining informed consent from the participants, relevant information was obtained using a validated semi structured proforma and the participants were assured of the confidentiality. The personal details of the participants were obtained. A brief history of presenting and past illnesses was obtained and a detailed clinical examination was done.

With all aseptic precautions 5.0 ml of venous blood was collected and the serum was separated. The Serum was stored in deep freezer at the Department of Biochemistry, Stanley Medical College. The hematological parameters were studied at the Department of Pathology, Stanley Medical College.

The following hematological indices were studied:

1. Hemoglobin levels
2. Red blood cell count
3. White blood cell count
4. Platelet count
5. Hematocrit (PCV)
6. Differential count of leukocytes
7. Mean corpuscular volume (MCV)
8. Mean corpuscular Hemoglobin (MCH)
9. Mean corpuscular Hemoglobin Concentration (MCHC)
10. Red cell distribution width (RDW)

The MELD (Model for End stage Liver Disease) score was calculated using the medscape calculator[6] by entering the values of serum creatinine, bilirubin and International normalized ratio (INR).

$$\text{MELD Score} = 10 \times ((0.957 \times \ln(\text{Creatinine})) + (0.378 \times \ln(\text{Bilirubin})) + (1.12 \times \ln(\text{INR}))) + 6.43$$

Statistical analysis: The collected data were entered in MS Excel and analysed. The categorical variables were expressed in frequency and percentage, and the continuous variables were expressed in mean and standard deviation. The correlation between the various hematological parameters and the MELD score was done using Pearson's correlation and correlation co-efficient (r) was calculated.

Results

Among the study population, 53 (88.33%) were males and 7 (11.67%) were females. 6 patients (10%) were under the age of 30 years, 44 (73.33%) patients were in the age group of 30-60 years and 10 (16.67%) patients were in the age group greater than 60 years.

Distribution of the cases of cirrhosis: It was found that Alcohol (Ethanol) induced decompensation was the commonest cause (63.33%) of cirrhosis among the study population followed by Hepatitis B (6.67%). (Table 1).

Table 1: Distribution of the causes of liver cirrhosis

Causes for Liver Cirrhosis	No of cases
Ethanol induced	38 (63.33%)
Hepatitis B	4 (6.67%)
Auto-immune	2 (3.33%)
Non-alcoholic steatohepatitis (NASH)	1 (1.67%)
Wilson's disease	2 (3.33%)
Chronic Budd chiari syndrome	2 (3.33%)
Biliary Cirrhosis	1 (1.67%)
Hepatocellular carcinoma	1 (1.67%)
Obstructive	3 (5%)
Cryptogenic	1 (1.67%)
Post-transplant	2 (3.33%)
EHPVO	1 (1.67%)
Non-specific	2 (3.33%)

Hematological indices in the patients with liver cirrhosis: The demographic characteristics and values of the various hematological indices of the study participants are shown in Table 2.

Table 2: Demographic and Hematological characteristics of the study population

Study Population (n) = 60	Mean ± SD
Age : Range (16-78)	44.83 ± 13.94
Gender	
Male	53 (88.33%)
Female	7 (11.67%)
Hematological parameters	
Hemoglobin (g/dl)	9.76 ± 2.61
RBC Count (million/cu.mm)	3.24 ± 1.13
WBC Count (× 10^3/cu.mm)	8.72 ± 4.04
Platelet Count (lakh/cu.mm)	1.7 ± 1.37
Hematocrit (%)	28.7 ± 7.78
MCV (fL)	90.57 ± 13.24
MCH (pg)	31.09 ± 5.7
MCHC (%)	33.52 ± 3.73
RDW (%)	17.63 ± 3.73
MELD Score	17.11 ± 8.4

It was found that 31 patients (51.67%) had hemoglobin values of less than 10g/dl among which 4 patients (4/60)(6.67%) were found to have hemoglobin less than 6g/dl. 3 patients (5%) had hemoglobin values of greater than 15 g/dl. 26 patients (43.33%) were found to have RBC count less than 3 million/cu.mm. 5 patients (8.33%) were found to have very low RBC count (<2 million/cu.mm) and all these 5 cases were ethanol induced. The hematocrit was less than 35% in 46 patients(76.67%) and greater than 45% in 2 patients (3.33%). All 38 patients (100%) with ethanol induced cirrhosis had hematocrit values less than 35%.

14 patients (23.33%) had WBC counts greater than 11,000/cu.mm and 4 patients (6.67%) had WBC counts less than 4,000/cu.mm. 9 patients of ethanol induced cirrhosis (9/38)(23.68%) had WBC counts greater than 11,000/cu.mm and 2 patients of HBV induced cirrhosis (2/4)(50%) had WBC counts greater than 11,000/cu.mm. 2 patients of ethanol induced cirrhosis (2/38)(5.26%) had WBC counts less than 4000/cu.mm.

In the differential count, 38 patients (63.33%) had neutrophils greater than 60% and 1 (1.67%) had neutrophils less than 40%. 68.42% (26/38) of ethanol induced cases had neutrophils greater than 60%. Decreased lymphocyte percentage (<20%) was found in 22 patients (36.67%) and increased lymphocyte percentage (>40%) was found in 4 patients (6.67%). 39.47 % (15/38) of ethanol induced cases had decreased lymphocytes (<40%).

33 patients (55%) were found to have thrombocytopenia (Platelet count <1.5 lakh/cu.mm) and 7 patients (7/60)(11.67%) had platelet count less than 50,000/cu.mm. 6 patients(6/38)(15.79%) with ethanol induced cirrhosis had platelet count less than 50,000/cu.mm.

The mean corpuscular volume (MCV) was less than 80fL in 9 patients (15%) and greater than 96fL in 16 patients (26.67%). Among ethanol induced cirrhosis cases, 14 patients (14/38)(36.84%) had MCV values greater than 96fL and 6 patients (6/38)(15.79%) had MCV values less than 80fL. The mean corpuscular hemoglobin (MCH) was less than 27pg in 13 patients (21.67%) and greater than 33pg in 16 patients (26.67%) Among ethanol induced cirrhosis cases, 6 patients (6/38)(15.79%) had MCH values less than 27 pg and 15 patients (15/38)(39.47%) had MCH values greater than 33pg. Both the auto-immune cases (2/2)(100%) had low MCH values(<27pg). The mean corpuscular hemoglobin concentration (MCHC) was less than 30% in 4 patients (6.67%). 2 patients with

ethanol induced cirrhosis (2/38)(5.26%) had MCHC values less than 30%.

The red cell distribution width (RDW) was increased (>14.5%) in 31 patients (51.67%). Among the ethanol induced cirrhosis cases, 21 patients (21/38)(55.26%) had RDW values greater than 14.5%. All the 4 cases (4/4)(100%) of HBV induced cirrhosis had RDW values greater than 14.5%.

Model for End stage Liver Disease (MELD) Score: The mean value of the MELD scores of the study population was 17.11 ± 8.4.

Correlation between the hematological parameters and MELD score: The correlation between the hematological parameters and MELD score was done and the correlation co-efficients (r) were tabulated (Table 3). Our study did not reveal any correlation between hematological indices and the MELD scores in patients with cirrhosis. It was found that Hemoglobin, RBC count, WBC count, Hematocrit, and Lymphocyte percentage in Differential count had very weak negative correlation (r = - 0.12, - 0.2, - 0.01, - 0.17, and - 0.05 respectively) with the MELD score while the RDW and platelet count had a weak negative correlation (r =- 0.28 and - 0.33 respectively). MCV, MCH, MCHC and Neutrophil percentage in Differential count had very weak to weak positive correlation (r = + 0.21, + 0.11, + 0.24 and + 0.03 respectively) with the MELD score.

Table 3: Correlation between hematological parameters and MELD Score

Hematological Parameters	Correlation co-efficient
Hemoglobin (g/dl)	-0.12
RBC Count (million/cu.mm)	-0.2
WBC Count (× 10^3/cu.mm)	-0.01
Platelet Count (lakh/cu.mm)	-0.33
Hematocrit (%)	-0.17
MCV (fL)	+0.21
MCH (pg)	+0.11
MCHC (%)	+0.24
RDW (%)	-0.28
Differential count (Neutrophils)	+0.03
Differential count (Lymphocytes)	-0.05

Discussion

Various abnormalities are common in most of the hematological parameters in patients with cirrhosis. The etio-pathogenesis of these hematological abnormalities is multi-factorial including variations in the factors stimulating bone marrow, sequestration of the blood cells due to portal hypertension, Hypersplenism, viral and toxin induced suppression of the bone marrow.[1]

Patients with portal hypertension are prone for occult or chronic bleeding associated with enteropathy which further leads to anemia. The consumption coagulopathy or the disseminated intravascular coagulation may contribute to thrombocytopenia in decompensated cirrhosis.[8] Abnormalities in the hematological indices are associated with increased risk of complications including infections and bleeding.[1,7] Recent studies have suggested that the abnormalities in the hematological indices are associated with a poor prognosis in the management of cirrhosis.[1,2,4]

Our study revealed that there were abnormalities in the different hematological parameters considered. Globally, viral hepatitis (Hepatitis B and C) is the commonest cause of liver cirrhosis whereas in India, alcoholic liver disease remains the commonest cause of cirrhosis. Our study also revealed that ethanol induced decompensation was the commonest cause (63.33%) for cirrhosis followed by Hepatitis B (6.67%) in a tertiary care hospital of South India. There were also cirrhosis cases caused due to Wilson's disease, Non-alcoholic steatohepatitis, Biliary cirrhosis, autoimmune hepatitis and even chronic Budd chiari syndrome.

The MELD scores of the study participants revealed that 45% (27/60) had 6% (score 10-19) mortality probability, 13.33% (8/60) had 19.6% (score 20-29) mortality probability and 8.33% (5/60) had 52.6% (score 30-39) mortality probability.[6,9,10] There was however no correlation with the MELD scores. However, as the presence of abnormalities in the hematological parameters is associated with a poor clinical outcome and it further increases the risk of bleeding and infections, the abnormalities in the hematological indices are to be effectively studied in detail in future which will aid in the appropriate management of cirrhosis and prevention of complications, thereby contributing to better prognosis. We also need further studies to assess the

root causes of these hematological abnormalities especially the factors affecting the bone marrow and the adverse effects of portal hypertension which deteriorate the clinical outcome of cirrhosis.

Conclusion

Although our study identified many abnormalities in hematological indices in the patients with cirrhosis, there was no correlation with the MELD scores. Further prospective and follow-up studies are to be done, preferably with a larger sample size, to evaluate whether the abnormalities in the hematological indices can be used as prognostic markers in the management of cirrhosis, thereby preventing the morbidity and mortality.

Acknowledgment: The authors express their gratitude to the Department of Medical Gastroenterology, Stanley Medical College, Chennai for help rendered.

Conflicts of interests: Nil

References

1. Qamar AA, Grace ND. Abnormal hematological indices in cirrhosis. Gastroenterol. 2009 Jun; 23(6): 441-445.
2. Demet B, Coskun O, Sevinc E. The evaluation of hematological indices for prediction of liver fibrosis in Chronic Hepatitis. BAOJ Gastro. 2017; 1(1):001.
3. Toghill PJ, Green S, Ferguson F. Platelet dynamics in chronic liver disease with special reference to the role of the spleen. J Clin Pathol. 1977; 30:367-71.
4. Qamar AA, Grace ND, Groszmann RJ. The incidence, prevalence and clinical significance of abnormal hematological indices in patients with compensated cirrhosis. Clin Gastroenterol Hepatol. 2009 Jun; 7(6):689-95.
5. Perz JF, Armstrong GL, Farrington LA, Hutin YJ, Bell BP. The contributions of hepatitis B virus and hepatitis C virus infections to cirrhosis and primary liver cancer worldwide. J. Hepatol. 2006 Oct; 45 (4): 529–38.
6. MELD Score for End-Stage Liver Disease. Available from url: ww.reference.medscape.com/calculator/meld-score-end-stage-liver-disease (accessed 19th September 2018).
7. Bacon BR. Cirrhosis and its complications. Harrison's Principles of Internal Medicine. 18th Ed. New York : McGraw Hill; 2015. p.2058-2066.
8. Morlock CG, Hall BE. Association of cirrhosis, thrombocytopenia and hemorrhagic tendency. Arch Intern Med. 72:69–77.
9. Kamath PS, Kim WR. The model for end-stage liver disease (MELD). Hepatology. 2007 Mar; 45 (3): 797–805.
10. Jung GE, Encke J, Schmidt J, Rahmel A. Model for end-stage liver disease. Der Chirurg. 2008; 79 (2): 157–63.