AN OBSERVATIONAL STUDY OF CLINICAL AND HEMATOLOGICAL PROFILE OF CIRRHOSIS OF LIVER

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ABSTRACT

Objective: Efforts can be made to normalize the hematological parameters so that the morbidity and mortality in these patients can be effectively reduced.

Methods: This observational study was carried out among 69 cirrhosis patients that fulfills the inclusion and exclusion criteria, attended the medicine outpatient department, and admitted in medicine ward of PRM Medical College and Hospital, Baripada, Dist. Mayurbhanj, Odisha, India, from June 2018 to January 2019.

Results: In our study, we had 59 male and 10 female patients with an average age of 49.8±13.19 years. About 92.75% of the patients were alcoholic. Abdominal distension (92.75%) and ascites (84.06%) were the most common presenting complaints. Pallor was present in 42 (60.87%) cases. Splenomegaly was present in 35 (50.72%) cirrhotic patients. Renal dysfunction was present in 23 (33.33%) cases. Sixty-six (95.65%) patients had anemia and 47 (68.12%) patients had thrombocytopenia.

Conclusions: From this study, we can conclude that, in cirrhosis of liver patients, various hematological changes are very common which need to be identified and corrected early to reduce morbidity and mortality.

Keywords: Cirrhosis, Anemia, Thrombocytopenia, Alcoholic, Non-alcoholic.

INTRODUCTION

The liver is one of the most complex functioning organs with a wide array of functions in human body. It plays a major role in carbohydrate, protein, lipid metabolism, synthesis of plasma proteins and maintenance of immunity (Kupffer cells), inactivation of various toxins, metabolism of drugs, and hormones. The liver has an extremely important role in maintenance of blood homeostasis as it functions as a storage depot for iron, folic acid, and Vitamin B12, secretes clotting factors and inhibitors. Hence, it is not surprising that, in liver diseases, a wide range of hematological abnormalities can be seen.

In general population, global prevalence of cirrhosis from autopsy studies ranges from 4.5% to 9.5% [1-3]. Hence, taking the adult population into count, we estimate that more than 50 million people in the world would be affected with chronic liver disease (CLD). At present, globally, the most common causative factors are alcohol, non-alcoholic steatohepatitis and viral hepatitis. The prevalence of cirrhosis is likely to be underestimated; as almost one-third of the patients remain asymptomatic.

During 2001, the estimated worldwide mortality from cirrhosis was 771,000 people; it was ranked 12th and 13th as the leading cause of death in the world and in developed countries, respectively [4]. Deaths from cirrhosis have been estimated to increase and would make it as the 12th leading cause of death in 2020 [5].

CLD in the clinical context is a disease process of the liver that involves progressive destruction and regeneration of the liver parenchyma, leading to fibrosis and cirrhosis [6].

CLD frequently associated with hematological abnormalities. Pathogenesis of hematomal changes is multifactorial and included portal hypertension induce sequestration, alteration in bone marrow stimulating factors, viral and toxin-induced bone marrow suppression, and consumption or loss.

Anemia of diverse etiology occurs in about 75% of patients of CLD [7]. Causes of anemia in CLD – iron deficiency, hypersplenism, anemia due to chronic disease, autoimmune hemolytic anemia, folic acid deficiency, aplastic anemia, and as an effect of antiviral drug. Alcohol is the most commonly used drug whose consequences include the suppression of hematopoiesis. These patients may suffer from nutritional deficiencies of folic acid and other vitamins due to malabsorption, malnutrition, or direct toxic effect that play a role in hematopoiesis. As a result, alcoholics may suffer from moderate-to-severe anemia, characterized by enlarged, structurally abnormal red blood cells (RBCs), mildly reduced numbers leucocytes and neutrophils, and moderately to severely reduced numbers of platelets [8].

Thrombocytopenia is common in CLD; mainly due to portal hypertension associated splenic sequestration, alteration in thrombopoietin, bone marrow suppression, consumptive coagulopathy, and increased blood loss. In CLD and cirrhosis, alterations in primary platelet hemostasis (platelet adhesion, activation and aggregation) have received less attention than changes in secondary hemostasis (coagulation). An increased intrasplenic platelet breakdown with variable roles of decreased platelet production and splenic pooling appears to be the most important determinants. Regarding the functional change, there is a decreased agreeability attributable to defective (transmembrane and intracellular) signaling, a storage pool defect and an upregulation of the inhibitory pathways [9]. Thrombocytopenia is associated with increased bleeding tendency in CLD patients, so early detection of thrombocytopenia is important and helpful for decreased mortality and morbidity.
Abnormalities in hematological indices are associated with increased risk of complications including bleeding and infection. Efforts can be made to normalize the hematological parameters so that the morbidity and mortality in this cirrhosis of liver patients could be effectively reduced. This could also extend help in increasing the longevity in transplant awaiting patients. We, through our study, have made an attempt to group the patients with deranged hematological indices and analyzed the variation of these indices in accordance. This could have clear therapeutic implications in managing these patients and reducing the adverse events.

METHODS

This observational study was carried out among 69 cirrhosis patients that fulfills the inclusion and exclusion criteria and attended the medicine outpatient department and admitted in medicine ward of Pandit Raghunath Murmu Medical College and Hospital (PRMMCH), Baripada, Dist. Mayurbhanj, Odisha, India, from June 2018 to January 2019. The following criteria were excluded from the study:

- Patients previously diagnosed to have one of the following causes of CLD
  - Primary biliary cirrhosis
  - Wilson’s disease
  - Hemochromatosis
  - Primary sclerosing cholangitis.

Patients of CLD presenting with associated comorbid diseases such as chronic renal failure and congestive heart failure
- Malignancy
- Pregnancy
- Previous history of hematological and coagulation disorder other than CLD
- Anemic patients already taking medications before being diagnosed as CLD.

After due consideration into inclusion and exclusion criteria, detailed history and clinical examination were undertaken in all subjects. Each subject instructed to have following investigations: Complete blood count (Sysmex XS-800i), USG abdomen, liver function tests, hepatitis B surface antigen, hepatitis C virus antibody, serum urea, and creatinine. Twenty healthy persons were taken as controls.

In the present study, anemia was defined using the World Health Organization definition hemoglobin (Hb) concentration <12 g/dl (females) and <13 g/dl (males). The severity of anemia was classified as mild anemia (Hb concentration between 11–12.9 g/dl for males and 11–11.9 g/dl for females); moderate anemia (Hb concentration between 8 and 10.9 g/dl) and severe anemia (Hb concentration <8 g/dl) [10]. Thrombocytopenia was defined with a value of <150×10^9/µl.

Statistical analysis

All the data were fed on Excel spreadsheet, and statistical analyses were made using the SPSS version 21.0 software. Results were expressed in average±standard deviation, frequencies, and percentages. Continuous data were compared using Student’s t-test. p<0.05 was considered as statistically significant for all tests conducted.

RESULTS

During the study period, 69 patients with cirrhosis of liver admitted in medicine ward of PRMMCH, Baripada, fulfill inclusion and exclusion criteria. All the cases were studied for the clinical presentation, risk factors, and laboratory parameters.
Our study group consisted of 69 patients of cirrhosis of liver, out of which 59 (85.51%) were male and 10 (14.49%) were female with the age range from 16 to 76. In our study, the average age of male patients was 50.05±13.04 years and of female patients was 48.3±14.74 years. The average age of the patients in the study was 49.8±3.19 years, which is comparable with the study by Suthar et al. [11] and Sarin et al. [12]. In our study, M:F ratio was 5.9:1, which are due to the cultural and traditional influences in our country. About 55.07% of the patients were between 40 and 60 years of age, which shows a high prevalence of this disease among the productive age group. In our study, abdominal distension (92.75%) and ascites (84.06%) were the most common presenting complaints.

In our study, abdominal distension (92.75%) and ascites (84.06%) were the most common presenting complaints. Ascites was also a common finding in the previous studies; Suthar et al. [11], Pathak et al. [12], and Mendenhall [14]. Splenomegaly was present in 35 (50.72%) patients of cirrhosis of liver in our study.

In a study by Suthar et al. [11], splenomegaly was seen in 60% of cases. Only 1 (1.45%) case presented with hepatic encephalopathy.

In our study, the blood urea was raised (>40 mg/dl) in 36.23% (25 cases) of the patients, indicating indirect injury to the renal injury (49.1%) in a study by Pathak et al. [13] and 37% in a study by Hegde et al. [15].

In our study, the creatinine was raised (>1.5 mg/dl) in 22 patients (i.e., 31.88% of the study group) which were comparable with 39.4% in a study by Pathak et al. and 20% in a study by Hegde et al. It was observed that 23 patients had glomerular filtration rate (GFR) <60 ml/min; thus, 33.33% of the patients had significantly reduced GFR. Hegde et al. studied that 30% of the patients had significantly reduced GFR.

The mean Hb level in our study was 7.99±2.18 g/dl, whereas in other studies, the findings were as Hegde et al. [9.12 g/dl]. In our study, we found that 66 (95.65%) of the patients had anemia, out of which 37 (53.62%) had Hb ≤8 g/dl, i.e. severe anemia. A study by Gonzalez-Casas et al. [16] showed that anemia in CLD patients was 75%. Hegde et al. study also found severe anemia in 43% of cases. In our study, 36.23% had normal mean corpuscular volume, 60.87% has microcytic blood picture, and 2.9% had macrocytic blood picture. Macrocytic anemia was more common in males than females. Microcytic hypochromic anemia was predominant in cirrhosis patients. This may be due to the low socioeconomic and poor nutritional status of most of the cases in this part of Odisha.

According to interesting article by Kojovich MD - “Hemostatic defects in end-stage liver disease,” critical care clinics 21 (2005) [17], mild-to-moderate thrombocytopenia occurs in 49-64% of patients with decompensated CLD. In our study, 47 (68.12%) patients had thrombocytopenia (<150 x10^9/L), out of which 23 (33.33%) patients had <100 x10^9/L
Table 6: Comparisons between hematologic indices of cirrhosis patients and controls

| Indices                                      | Cirrhosis patients (mean±SD) (n=69) | Controls (mean±SD) (n=20) | p-value |
|----------------------------------------------|-------------------------------------|---------------------------|---------|
| Hemoglobin                                   | 7.99±2.18                          | 12.5±2.93                 | <0.0001 |
| Red blood count (M=4.7–6.1 and F=4.2–5.4)   | 3.15±0.90                          | 5.2±0.75                  | <0.0001 |
| Mean corpuscular volume (80–100)             | 76.12±12.01                        | 7.86±1.074                | 0.4023  |
| Packed cell volume (M=40.7–50.3 and F=36.1–44.3) | 23.92±6.99                        | 27.0±20.34                | 0.2724  |
| Mean corpuscular hemoglobin (27–31)          | 25.38±3.74                         | 26.1±14.26                | 0.482   |
| Mean corpuscular hemoglobin concentration (33.4–35.5) | 33.49±6.24                        | 34.0±1.29                 | 0.6714  |
| Red blood cell distribution width (11.5–14.5) | 17.28±2.40                         | 15.3±1.23                 | 0.0008  |
| Total platelet count (1.5–4.5)               | 1.38±0.79                          | 1.9±0.36                  | 0.0055  |
| Serum bilirubin total                        | 3.78±5.74                          | 0.72±0.45                 | 0.0199  |
| Serum bilirubin direct                       | 1.86±2.62                          | 0.3±0.25                  | 0.0138  |
| Serum glutamic pyruvic transaminase          | 75.45±79.68                        | 39.58±14.69               | 0.0491  |
| Serum glutamic oxaloacetic transaminase      | 99.46±11.95                        | 60.08±22.44               | 0.1356  |
| Alkaline phosphatase                         | 128.6±68.80                        | 72.3±24.30                | 0.0029  |
| Blood uma (10–40 mg/dL)                      | 44.19±53.08                        | 2.6±28.75                 | 0.1525  |
| Serum creatinine (0.5–1.3 mg/dL)             | 1.5±1.51                           | 1.15±0.12                 | 0.2658  |

SD: Standard deviation

In our study, the hematological parameters (Hb, RBC, and platelet) in cirrhosis of liver patients were statistically significant (p<0.05) (Table 6).

CONCLUSIONS

Many conclusive results regarding the hematological abnormalities in cirrhosis of liver were obtained with this limited study involving 69 patients with decompensated cirrhosis. The results of this study established most of the known facts about chronic alcoholic liver disease in this part of the world. Numerous clinical observations support the notion that alcohol adversely affects the production and functioning of virtually all types of blood cells. Long-term excessive alcohol consumption leads to liver cirrhosis which interferes with various physiological, biochemical, and metabolic processes involving the blood cell production and maturation, leading to these adverse effects. Not only liver function tests, patients with alcoholic liver disease have abnormal hematological and renal function too. Renal dysfunction is common in alcoholic liver disease, especially in patients with ascites. From this study, we can conclude that, in cirrhosis of liver patients, various hematological changes are very common which need to be identified and corrected early to reduce morbidity and mortality.

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AUTHORS’ CONTRIBUTIONS

Dr. Bibhu Prasad Behera, Assistant Professor in Medicine, Department of Internal Medicine, Saheed Laxman Naik Medical College and Hospital, Koraput, Odisha, is the primary investigator. Dr. Manoranjan Dash, Assistant Professor in Pulmonary Medicine, Saheed Laxman Naik Medical College and Hospital, Koraput, Odisha, is the corresponding author.

CONFLICTS OF INTEREST

None.

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ETHICAL APPROVAL

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