ORIGINAL ARTICLE

Anaemia Spectrum within Chronic Liver Disease: A Descriptive Analysis

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Abstract

Background: Chronic liver disease (CLD) is often associated with hematological abnormalities, affecting approximately 75% of patients. This condition may be exacerbated by deficiencies in folic acid and Vitamin B12, potentially due to inadequate dietary intake or malabsorption. **Aim:** This study aimed to evaluate the severity and type of anemia in CLD patients without overt bleeding for over 90 days, to improve management strategies and reduce related morbidity and mortality. Objective: Conducted at the Gastroenterology Department of Government General Hospital, Guntur Medical College, Andhra Pradesh, this year-long observational study took place from April 2022 to May 2023. We included 100 patients with CLD and anemia, all with hemoglobin levels above 10 g/dL and no recent bleeding episodes. **Result:** It was observed that in ALC the most common anaemia is folic acid deficiency (39.7%) followed by Iron deficiency (37.2%), in HBV Iron deficiency (54.5%) followed by Folic acid deficiency (36.4%), in HCV both Iron and Folic acid deficiency were equally distributed (42.9%) and in NAFLD Iron and B12 deficiency were equally distributed (25%). Regarding severity, about 14% were severely anaemic flowed by 63% moderately anaemic and 23% were mild anaemic as noticed. **Conclusion:** The majority of patients are middle-aged (40–60 years), the family experiences severe psychological, social, and financial hardship.

Key words: Alcoholic liver cirrhosis, fatty liver disease, folic acid deficiency, hepatitis b virus, hepatitis-c virus, iron deficiency, non-alcoholic etc

INTRODUCTION

As it is a known fact, the liver is crucial to healthy erythropoiesis, particularly to the production and breakdown of red blood cells (RBCs). Hematological anomalies are often linked to chronic liver disorders. Acute or chronic gastrointestinal (GIT) hemorrhages[1] are among the causes of anemia. Anemia of various etiologies affects around 75% of those suffering from persistent liver illness[2] as well as hypersplenism brought on by portal hypertension. Severe hypovolemia brought on by an acute hemorrhage might lead to secondary iron deficiency (ID) anemia. The most frequent hematological abnormality in cirrhosis patients is thrombocytopenia, which is closely followed by leukopenia and anemia.[3]

Furthermore, thrombocytopenia and/or reduced blood coagulation due to a lack of hepatocyte-synthesized blood coagulation factors predisposes severe hepatic illness patients to bleeding. Hepatitis development may be followed by anemia with aplastic traits, characterized by pancytopenia and hypocellular bone marrow.[4,5] Moreover, the most frequent hematological anomaly observed in cirrhosis patients is thrombocytopenia, which is closely followed by leukopenia and anemia.[6] It manifests as hemorrhagic symptoms and increasing anemia. Anemia during combination therapy for hepatitis C virus (HCV) infection can occur for a number of reasons, and ribavirin and/or interferons may be

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involved in the anemia process. In this case, hemolysis brought on by ribavirin is the primary cause of decreased hemoglobin concentrations.[7] It is possible to reverse ribavirin-induced hemolysis by either cutting back on dosage or stopping the medication completely. Interferons have the potential to cause anemia by suppressing bone marrow. Consuming alcohol has been linked to the development of chronic liver disease (CLD) and may also be a factor in the anemia that results from it.

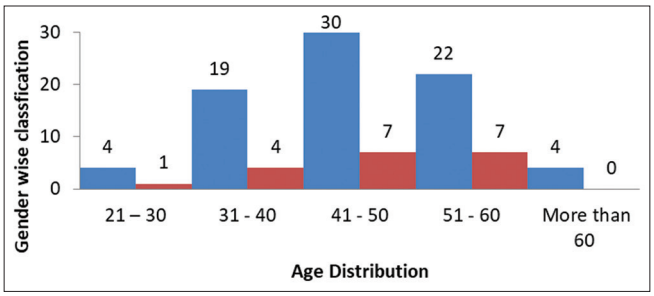

Figure 1: Age and gender-wise distribution

Table 1: Age and gender distribution

S. No.	Age (years)	Gender percentage		Total percentage
		M	F	
1	21–30	4	1	5
2	31–40	19	4	23
3	41–50	30	7	37
4	51–60	22	7	29
5	>60	4	0	6
	Total	81	19	100

Deficiency in folic acid and/or Vitamin B12, which can result from insufficient food intake or malabsorption, can worsen anemia in people with CLD. A number of additional causes contribute to the anemia, such as blood dilution brought on by an increase in plasma volume and splenic RBC pooling, which, depending on the size of the spleen, can trap up to 25% of the total mass of RBCs in circulation. In addition, there is a 50% reduction in red cell survival, which is likewise correlated with spleen size. An inadequate response of the bone marrow to anemia could be a contributing factor, depending on the underlying cause of portal hypertension. 66–75% of patients with hepatic cirrhosis may exhibit anemia.[8] To determine the type and degree of anemia, we assessed individuals with CLD who had anemia but had not experienced overbleeding within the previous 3 months.

MATERIALS AND METHODS

The study was carried out in the Government General Hospital in Guntur, A P., and the gastroenterology department of Guntur Medical College. Observational research lasting a year was carried out between April 2022 and May 2023. The frequency of patients with CLD admitted to the gastroenterology department was found to be 50%, according to hospital census data. The amount of the sample was determined by the formula N = 4PQ/L2, where *P* = 50%, Q is equal to 100-*P*, or 50%, and L is equal to the 20% allowable error in "*P*," or 10%, resulting in *n* = 100. All patients with clinically established CLD and anemia (hemoglobin [Hb] levels <10 g/dL) who did not have bleeding episodes in the previous 3 months who were admitted to the ward while the aforementioned time was

Table 2: Classification of anemia CCD patients

Etiology of a use of CLD	Etiology of anemia											
	BD		FD		FD+BD		IDA		IDA+BD		IDA+FD	
	Frequency	%	Frequency	%	Frequency	%	Frequency	%	Frequency	%	Frequency	%
ALC	6	7.7	31	39.6	3	3.8	29	37.3	1	1.4	8	10.4
HBV	0	0.0	4	36.5	0	0.0	6	54.6	0	0.0	1	9.2
HCV	0	0.0	3	43.0	0	0.0	3	42.8	0	0.0	1	14.2
NAFLD	1	25.0	1	25.0	0	0.0	1	25.0	0	0.0	1	25.1

CLD: Chronic liver disease, ALC: Alcoholic liver cirrhosis, HBV: Hepatitis B virus, HCV: Hepatitis C virus, NAFLD: Non-alcoholic fatty liver disease

Table 3: Distribution of grading and severity of anemia

Hb	Gender				Total	
	Male		Female			
	Frequency	%	Frequency	%	Frequency	%
<6 (Severe)	3	15.7	11	13.7	14	14.0
6–8.9 (Moderate)	12	63.1	51	63.1	63	63.0
9–12.9 (Mild)	4	21.2	19	23.4	23	23.0
Total	19	100.0	81	100.0	100	100.0

Hb: Hemoglobin

Table 4: Different types of chronic health diseases

Age years	Etiology							
	ALC		HBV		HCV		NAFLDa	
	Freq	%	Freq	%	Freq	%	Freq	%
21–30	3	3.8	1	9.1	0	0	1	25.0
31–40	20	25.6	1	9.1	2	28.6	0	0
41–50	28	35.9	4	36.4	3	42.9	2	50.0
51–60	21	26.9	5	45.5	2	28.6	1	25.0
>60	6	7.7	0	0	0	0	0	0

ALC: Alcoholic liver cirrhosis, HBV: Hepatitis B virus, HCV: Hepatitis C virus, NAFLDa: Non-alcoholic fatty liver disease

Table 5: Factors associated with CCD-averages

Variable	Etiology							
	ALC		HBV		HCV		NAFLD	
	Average	S D	Average	S D	Average	S D	Average	S D
AGE	47.3	10.1	47.3	8.8	47.4	7.2	45.0	13.3
TB	4.5	6.1	2.3	2.9	2.8	3.2	1.9	1.1
AST	82.8	70.8	44.2	24.2	71.4	59.0	65.5	18.6
ALT	47.7	39.8	31.7	27.4	54.0	39.8	32.5	5.3
ALBUMIN	4.3	12.9	3.0	0.6	2.9	0.5	2.7	0.3
PT INR	1.9	0.5	1.8	0.3	1.9	0.3	1.9	0.4
Hb (gr/dL)	7.9	1.5	6.8	1.6	6.9	1.7	7.2	2.3
MCH (pg)	26.9	4.7	26.9	4.4	26.3	3.9	23.5	5.5
MCV (fl)	93.2	14.6	86.3	15.4	90.1	10.2	91.3	20.9
Serum Folic acid (ng/mL)	5.2	2.5	5.1	3.3	4.6	2.6	6.9	3.2
SERUMb VitB12 (pg/mL)	431.0	221.3	536.1	232.6	494.9	174.4	400.8	224.3
S.iron	53.7	45.3	50.9	54.5	29.3	24.6	44.8	46.6
Ferritin	178.9	196.6	214.3	267.1	77.0	83.0	147.8	209.1
TIBC	447.2	87.9	412.6	82.9	470.6	82.1	457.5	65.1
CTPSCORE	8.7	2.2	7.5	2.1	8.7	1.9	9.7	2.2
MELD–NA	21.9	8.1	16.3	6.2	22.1	7.1	19.3	10.2

ALC: Alcoholic liver cirrhosis, HBV: Hepatitis B virus, HCV: Hepatitis C virus, NAFLDa: Non-alcoholic fatty liver disease, CDD: Chronic liver disease

included in the study after consent was obtained, up to the necessary sample size. Below is a summary of the inclusion and exclusion criteria, along with a thorough explanation of the study's methodology and objectives. Qualifications for inclusion: (1) age >18. (2) All patients with Hb levels <10 g/dL who suffer from CLD. First, you must be younger than 18. (3) Individuals who have experienced melena or hematemesis with overt bleeding within the last 3 months. (4) Individuals with confirmed hepatocellular carcinoma or GIT cancer. (5) Individuals suffering from coagulation or hematological disorders. (6) Acute CLD decompensation. (7) Liver failure not related to primary liver causes, such as septicemia or endotoxemia. One of the study's goals was to determine the sociodemographic characteristics of the participants. (8) To investigate the nature, etiology, and degree of anemia in the range of long-term liver diseases. The study was launched after the institution's ethical committee's approval. The necessary data were gathered using a pretested proforma that included information on the subjects' sociodemographic profiles, the kind, severity, and grading of anemia across the range of long-term hepatic dysfunction, as well as factors that were linked to various forms of CLDs. Every instance (study subject) in the research was overseen and followed through till they were released.

Finally, the gathered data were examined using computer software and suitable statistical methods such as percentages, proportions, central tendency, and dispersion measures. The study's findings were contrasted and examined to previously published research on related topics by other authors, which led to the formulation of conclusions and suggestions.

RESULTS AND DISCUSSION

Males made up the majority of study participants (81%) in contrast to females (19%). The research participants' average age was 46.7 years. Overall, it was found that people with CLD were mostly between the ages of 41 and 60 [Figure 1, Table 1].

Lack of folic acid (39.7%) and ID (37.2%) were found to be the most common anemias in alcoholic liver cirrhosis (ALC), hepatitis B virus (HBV), and non-alcoholic fatty liver disease (NAFLD), respectively. ID (54.5%) and folic acid deficiency (36.4%) were the most common anemias in HCV, and both deficiency (42.9%) and B12 and ID (25%) were equally distributed. ID anemia was the most prevalent kind of anemia that was found [Table 2].

In terms of severity, it was observed that roughly 14% of the population was extremely anemic, followed by 63% of those who were moderately anemic, and 23% of those who were mildly anemic [Table 3].

In this study, the largest number of ALC cases – 35.9% belongs to the age range of years 41–50. This was followed by 45.5% of HBV cases, 42.9% of HCV cases, and around 50% of NAFLD cases, which belong to the age group of 41–50 years. Overall, it was found that people with CLD were mostly between the ages of 41 and 60. The bulk of research participants belonged to the ALC spectrum of CLD; this was succeeded by NAFLD, HBV, and HCV [Table 4].

Participants in the study were 46.7 years old on average. The study indicated that when comparing HCV patients to ALC cases, the mean values of blood iron (29.29 mcg/dL), folic acid (4.59 ng/mL), and Vitamin B12 (221.3 pg/mL) were lowest in HCV cases.

The majority of the participants in this study were male (81%) as opposed to female (19%), which is consistent with the findings of studies by Rauf *et al*. (2014) and Kumar *et al*. (2014). The majority of patients are in the 41–60 year age range, and the mean age of 46.7 years is similar to studies by Patel and Shah[9] and Frijo Jose *et al*.[10] In our scenario, men are more likely than women to develop CLD after the age of 40 due to alcohol abuse and extramarital sex. The bulk of research participants fell into the ALC category when it came to the distribution of the spectrum of CLD, which was consistent with the findings of Kurundkar *et al*. that the order of prevalence was HBV, HCV, and NAFLD.

Folic acid deficiency (39.7%) was the most common anemia in ALC, followed by ID (37.2%); ID (54.5%) was the most common anemia in HBV, followed by folic acid deficiency (36.4%); the distribution of lack of iron and folic acid was equal (42.9%) in HCV; and in NAFLD, the distribution of iron and B12 deficiency was equal (25%). ID anemia was the most prevalent type of anemia found in this investigation, and other studies reporting comparable results included Özatli *et al*.[11] (2011), Manrai *et al*.[12] (2012), and Gkamprela *et al*.[13] (2013). Whether or not anemia is present, ID is linked to a number of symptoms and consequences that negatively affect patients significantly. It can lower the quality of life,[14] impair cognition, and increase cardiovascular morbidity and mortality.[14] In addition to raising the chance of dying, anemia raises the likelihood of hospitalization and acute chronic liver failure in individuals with alcoholic liver cirrhosis. Nutritional deficits, such as those in iron, Vitamin (Vit) B12, B6, and folate, are also common in patients with cirrhosis (Scheiner *et al*.[8]). The results of our study, which agreed with those reported by Kumar *et al*. (2014), Kurundkar *et al*., and Patel and Shah[9] investigations, indicated that approximately 14% of participants had severe anemia, followed by 63% with moderate anemia and 23% with mild anemia. Our investigation's mean hemoglobin concentration of 7.7 g/dL is in line with Anbazhagan *et al*. findings. Furthermore, the lowest mean blood iron (29.29 mcg/dL), folic acid (4.59 ng/mL), and serum Vitamin B12 (221.3 pg/mL) were found in ALC patients in this investigation, likely due to the fact that B12 insufficiency is widespread among alcoholics. Furthermore, the mean serum ferritin level was lowest (77 ng/mL) by Anbazhagan G *et al*,[15] in cases of HCV chronic liver, which is in line with the findings of studies by Intragumtornchai *et al*.,[16] Lipschitz *et al*.,[17] Nelson *et al*.,[18] and Guyatt *et al*.[19] Furthermore, HCV and NAFLD cases had lower albumin levels, which is in line with the findings of Scheiner *et al*. [Table 5].

Limitations of the study

- The study was conducted in a hospital; as a result, we were unable to obtain the study subjects' disease progression chronology after their release
- Not every instance was suitable for a bone marrow biopsy. There was just a serum folic acid test. If RBC folate levels are additionally included, the study may be improved
- To rule out an active parasite infection, we only examined the stool for 3 days in a row. We are very sensitive yet have low specificity.

CONCLUSION AND RECOMMENDATION

Since most patients are in the middle age range (40–60 years old), which has a major negative social impact on the family, economic, and psychological elements, it is crucial to concentrate on the disease's preventive aspects as soon as possible to minimize loss. This is because the majority of the factors that cause CLD are preventable. In addition, it is critical to encourage people to get vaccinated against HBV and HCV and to raise public knowledge of the negative impacts of alcohol consumption habits through health professionals' education, print, electronic, and social media outlets. In addition, it is recommended that patients with a

history of heavy alcohol consumption and HBV and HCV viral infections be prescribed iron and folic acid pills and B-complex or multivitamin supplements as soon as possible to treat and avoid anemia.

To prevent or limit the progression of CLD and thereby lower the morbidity and mortality associated with it, people who have a family history of NAFLD, habituate alcohol consumption and are positive for HBV or HCV should have periodic liver screenings.

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