Section: General Medicine

Original Research Article

ANEMIA IN LIVER CIRRHOSIS AS A RISK PREDICTOR OF DEVELOPMENT OF ASCITES

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Abstract

Background: Anemia and hypoalbuminemia are considered independent risk factors for morbidity and mortality in cirrhosis. Yet there is insufficient data on the correlation between hemoglobin, serum albumin, nutritional status, and the risk of developing ascites in patients with cirrhosis. The study aims to evaluate hemoglobin as an early risk predictor for hypoalbuminemia and thus ascites. **Materials and Methods:** This was a retrospective study. A total of 58 liver cirrhosis patients from January 2019 to December 2021 were studied. The medical records were reviewed manually for prospective changes in hemoglobin, serum albumin, and ascites at each visit. Patients were grouped into mild, moderate, and severe anemia groups against serum albumin levels, and the development of ascites was evaluated. **Result:** All 58 patients studied developed anemia, hypoalbuminemia, and ascites within two years. The decrease in hemoglobin from 14.7g/dl to 8.89g/dl and albumin from 3.9g/dl to 2.26g/dl strongly correlated with the development of ascites in all patients r (56) =.72, p = .00001. The onset of anemia in cirrhosis could assist in the early prediction of the risk of hypoalbuminemia and thus ascites, R^2 = .00079, F (1, 56) = 0.044, p = .834, β = .0056, p = .834, α = 4, p = .001. **Conclusion:** Anemia being a common complication in liver cirrhosis can be applied as an early predictor for the risk of developing hypoalbuminemia and thus, ascites and the observed association between anemia and albumin warrants further research.

INTRODUCTION

Anemia is the most common complication encountered in more than 80% of patients with cirrhosis patients. The causes of anemia in chronic liver cirrhosis are related to disease-affected organs, nutrient depletion, endocrine disturbances, and metabolic changes. The cause of anemia in chronic liver diseases includes reduced protein and energy intake through the diet, gastrointestinal bleeding, defective synthesis of blood cells and coagulation proteins, and liver enzyme disturbances. The prevalence of anemia is observed in more than 75% of liver cirrhosis patients.[1] 22% of compensated and 78% of decompensated cirrhosis patients develop anemia due to altered iron and protein metabolism in the liver.[2] Most of the patients in the hepatic wards are managed with blood transfusions, and multiple transfusions have a risk for iron overload, thereby increasing the risk of morbidity and mortality.[3]
Depending on the hepatic complications and their influences on the RBC morphology, the involvement of spleen and bone marrow in cirrhotic patients, anemia has always been a challenge in management due to different causative factors in anemia, a type of anemia, and changes in RBC morphology, and hepcidin, spur cells.[4,5] Generally, severe anemia is seen in most protein and energy-deficit malnourished patients who develop pot-belly, i.e., with ascites caused due to hypoalbuminemia associated with poor protein status.[6-12] Similarly, protein metabolism is affected in cirrhosis due to loss of protein digestibility, reduced absorption capacity, decreased protein synthesis, and metabolism by the liver.[13-16] Anemia is associated with a significant risk of hepatic decompensation and mortality. Although anemia and hypoalbuminemia with ascites are present in more than 80% of the decompensated liver cirrhosis population, studies on related associations between them are insufficient. In this study, we intended to understand the risk of ascites with decreasing levels of hemoglobin and serum albumin and to evaluate anemia as an early sign predictor of the development of hypoalbuminemia and ascites.[17-20]

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MATERIALS AND METHODS

Study design and setting

The study was a retrospective analysis of data from the health records of the chronic liver cirrhosis patients admitted under the General Medicine unit at R L Jalappa Hospital in Kolar, between January 2019 and December 2021.

Eligibility Criteria

Patients over 18 years, both genders diagnosed with chronic liver cirrhosis having normal ranges of hemoglobin, serum albumin, and body mass index were included. We excluded patients with hemoglobin in the anemia range (less than 13 g/dL for males and less than 12 g/dL for females (WHO criteria) upon the first hospital admission. The patients' records had acute medical conditions that may cause or contribute to the decrease in hemoglobin, which included gastrointestinal bleeding, transfusion history, a previous history of anemia, chronic kidney disease, surgeries, or any comorbidities treated with medications that may affect hemoglobin levels were also excluded.

Data sources and measurements

Demographics, diagnosis, BMI, and laboratory data for each patient were extracted from the health records and measured upon arrival at the medical admission unit. Charts were manually reviewed, ensuring systematic and complete follow-up documentation. Records were studied and data were extracted for changes in weight, hemoglobin, serum albumin, and fluid accumulations in the abdominal cavity at each visit to hospitalization. The presence of edema and ascites was confirmed by abdominal ultrasound recordings in the chart. We divided the patients into three predefined groups according to their hemoglobin (>13, 8-12, and <8g/dl) and plasma albumin levels (0–34, 35–44, and ≥45 g/L) at each visit. Using the discharge diagnoses from the preceding admissions, we calculated the Charlson Comorbidity Score as a marker for comorbid illness and to evaluate the risk factors for anemia and hypoalbuminemia.

Ethics

The Institutional Ethics Committee has approved the study as per the research rules and regulations. No written informed consent was required in this study.

Statistical Analysis

All data were presented as mean ± standard deviations, and or proportions (%). A linear regression analysis was carried out on the predictive power of hemoglobin where the outcomes were hypoalbuminemia and ascites with anemia being the exposure event. Relative risk and Pearson's correlation coefficient analysis was performed to clarify the ability of hemoglobin to identify patients at an increased risk of developing hypoalbuminemia and thus ascites. The level of significance was set at $P < 0.05$.

RESULTS

Characteristics of the patients: Between January 2019 and December 2021, a total of 91 liver cirrhosis patients hospitalized in the general medicine department were reviewed. Thirty- three of ninety-one patients' records were excluded due to hemoglobin in the anemic range at first hospital admission. Fifty-eight patients with normal hemoglobin and serum albumin at the first visit were included in the study. Of the 58 health records included, 54 (93.10%) were male and 4 (6.89%) were female patients with a mean age of 49 years (49.16 ±10.47 years). Etiology was 96.55% alcoholic (n=56) and 3.44% NAFLD (n=2). At baseline, BMI was 19.2 kg/m², and the median overall Charlson comorbidity index at the baseline was 1 (0–3), which progressed to 3.5 (3-6) in the range of 16-21 months in 43 patients (74.13%). Patients' characteristics were compared based on the anemia group as independent variables, while serum albumin and ascites as dependent variables, after adjusting all the confounding variables and cirrhosis-related comorbidities in the final analysis. [Table 1]

After adjusting the age, sex, comorbidities, and BMI, we found that the two main factors that can predict the drop in hemoglobin in hospitalized patients were the severity of the disease and BMI. Charlon's comorbidity index, median score, and IQR were 3.5 (1-6). In patients with normal BMI 19.2 kg/m², mean hemoglobin was 14.2 ±1.98 g /dl ($P < 0.0001$) in male patients, while females had Hb =12.68 ± 0.45g/dl ($P < 0.0010$) and mean serum albumin was 3.92 ±0.39 g /dl (P<0.0002). BMI reduced by 2 -5 kg/m² within 3-6 months and 61% of patients (37 patients) had dropped their hemoglobin by 1.0 -3.2 g/dL ($P < 0.0001$) with a drop in serum albumin by 0.2 - 0.7g/dl ($P < 0.0001$) and BMI further drop by 4 – 6 kg/m² (14-16kgs/m²) in the year. While 72.22% of the male (39 patients) with mild anemia (12g/dL) developed moderate anemia (<10g/dl) and 100% of the female (4 patients) with moderate to severe anemia (<8g/dl) within six to eight month. All these patients had dropped their serum albumin below 3g/dl with signs of abdominal distention and the presence of ascites, confirmed by USG scan. The remaining 27.8% of males (n=15) were at borderline anemia with serum albumin levels between 3.1 -3.3g /dl around one year and later become severely anemic. The BMI of these male patients was within normal 22.7 kg/m². By the end of the two-year follow-up, severe anemia, hypoalbuminemia, and ascites developed in all fifty-eight. 38% of patients had received blood transfusions and 100% had undergone therapeutic paracentesis. However, the difference in the rate of anemia and hypoalbuminemia by gender was not significant ($P = 0.342$). On average at each hospital visit, men and women dropped hemoglobin by 1.6 g/dL and 1.4 g/dL, respectively. Albumin levels were analyzed, and the mean plasma albumin was 3.92 g/dL. Patients with low hemoglobin <12g/dl had

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albumin <3.4 g/dL, (p<0.0001) and were admitted longer (p<0.001). With every 1-1.2 g /dl drop in hemoglobin, noted that serum albumin dropped by 0.2 to 0.3g/dl irrespective of gender. BMI decreased below 16.50 kg/m² when Hb dropped to below 10g/dl, and SA below 3.0g/dl. 71% of patients were diagnosed with mild ascites along with pedal edema at Hb level 12g/dl and SA level of 3.2g/dl (p= 0.00001). Moderate to severe ascites were present in patients with Hb and SA levels dropped below 8g/dl, and 2.9g/dl respectively. A Strong positive correlation r (56) =.72, p = .00001 showing that albumin values were low with low hemoglobin values. Linear regression analysis showed predictive co-relation of hemoglobin to hypoalbuminemia, R^2 = .00079, F (1, 56) = 0.044, p = .834, β=.0056, P=.834, α=4, P= <.001 (Figure 1, 2 and 3). The above analysis supported that serum albumin varied with hemoglobin levels. [Table 2]

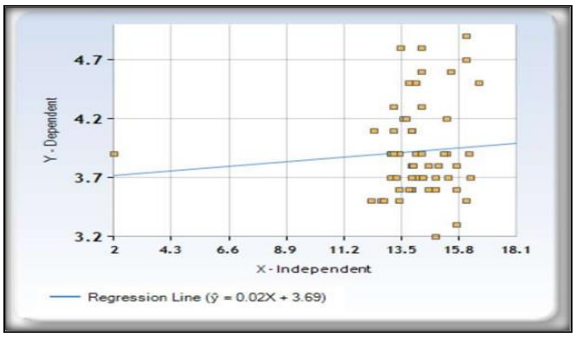

Figure 1: Correlation of hemoglobin and serum albumin

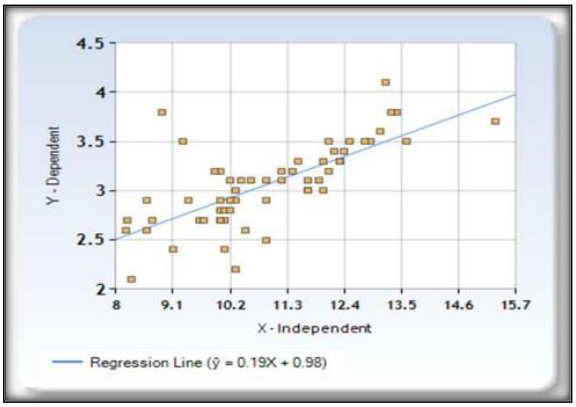

Figure 2: Correlation of hemoglobin and serum albumin

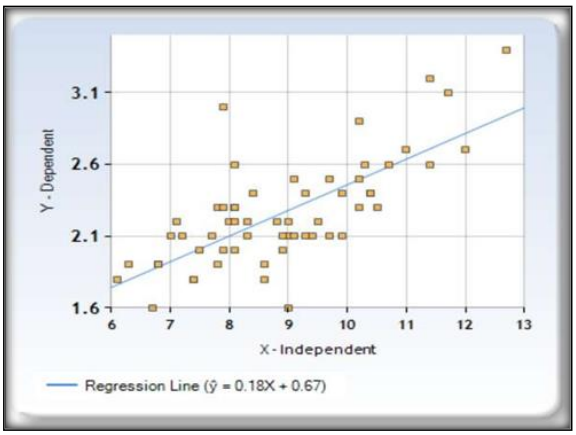

Figure 3: Correlation of hemoglobin and serum albumin

Y is serum albumin (dependent variable) and X is hemoglobin (independent variable) at baseline, 3 months, and 6 months.

Table 1: Clinical and biochemical characteristic data of the patients

Patient's characteristics	Baseline	3 months	6 months	P-value
Age (years)	49.16 ±10.47	-	-	-
BMI (kg/m²)	24.6 ± 3.7	21.0 ±1.9	16.9 ±1.3	0.0030
Child-Pugh Score and Class	9.4 ± 1.5	11.0 ± 1.2	14.0 ± 1.1	0.1622
Hb (g/dl)	14.2 ±1.98	10.9 ±1.55	8.89 ±1.49	0.0001
Serum albumin (g/dl)	3.92 ± 0.39	3.06 ± 0.41	2.26 ± 0.37	0.0001
Total proteins (g/dl)	7.53 ± 0.69	6.86 ± 0.77	6.16 ± 1.05	0.0760
Serum creatinine (mg/dl)	0.53±0.22	1.0 ± 0.6	1.1± 0.7	0.5819
Blood Urea Nitrogen (mg/dl)	17.9± 10.1	21.4 ± 11.7	29.3 ± 19.2	0.1839
Charlson's comorbidity score	1	3	4	0.0491

Table 2: Mean values of clinical parameters and relative risk*

Timeline	BMI	HB	SA	AF	R-value	p-value**
Baseline	19.20	14.1	3.92	0	0.0837	0.5321
3 months	17.88	10.9	3.06	2	0.7119	0.00001
6 months	16.52	8.89	2.26	3	0.7165	0.00001

*Abbreviations: BMI – body mass index, HB- Hemoglobin, SA- serum albumin, AF- ascitic fluid, R-value =Pearson's correlation coefficient. **p-value < 0.05 is statistically significant.

DISCUSSION

Hemoglobin values <12 g/dl had serum albumin values <3.2g/dl, (p <0.000) had a significant risk for ascites than patients with normal hemoglobin and albumin. Anemia is an independent risk factor for hepatic decompensation and mortality in patients with cirrhosis. However total proteins did not have any significance in Hb, SA, and BMI. With each percentage drop in Hb and a simultaneous drop in albumin patients, we noticed a higher risk of developing ascites. The lacunae in our study were the presence of a few compounding factors like the worsening of anemia with severity of disease,

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reduced nutrition intake, gastrointestinal bleeding, and varices as demonstrated by the Charlson comorbidity index. The number of patient visits was also limited due to COVID-19 during the period. Further prospective larger studies are needed to overcome the limitations in the sample size, and compounding variables and to validate the results.[21,22]

CONCLUSION

With higher incidences of anemia of chronic diseases in patients with decompensated liver cirrhosis patients. We found that serum albumin levels decreased with decreasing hemoglobin levels resulting in ascites. Our study demonstrated that anemia could be used as an early risk predictor for hypoalbuminemia and thus ascites. Since the study is retrospective, further studies are needed to evaluate the impact of anemia and hypoalbuminemia on the development of ascites in patients with cirrhosis. It is important for an understanding of this relationship for early detection and intervention, to improve patient outcomes.

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REFERENCES

1. Scheiner B, Semmler G, Maurer F, Schwabl P, Bucsics TA, Paternostro R et al. Prevalence of and risk factors for anemia in patients with advanced chronic liver disease. *Liver International*. 2020 Jan;40(1):194-204.
2. Weiss G, Goodnough LT. Anemia of chronic disease. New England Journal of Medicine. 2005 Mar 10;352(10):1011-23.
3. Gonzalez-Casas R, Jones EA, Moreno-Otero R. Spectrum of anemia associated with chronic liver disease. World Journal of Gastroenterology: WJG. 2009 Oct 7;15(37):4653.
4. Paternostro R, Kapzan L, Mandorfer M, Schwarzer R, Benedikt S, Viveiros A et al., Anemia and iron deficiency in compensated and decompensated cirrhosis: Prevalence and impact on clinical outcomes. Journal of Gastroenterology and Hepatology. 2020 Sep;35(9):1619-27.
5. Singh S, Manrai M, Parvathi VS, Kumar D, Srivastava S, Pathak B. Association of liver cirrhosis severity with anemia: does it matter. Annals of Gastroenterology. 2020 May;33(3):272.
6. Kowdley KV. Iron overload in patients with chronic liver disease. Gastroenterology & hepatology. 2016 Nov;12(11):695.
7. Paternostro, R., Kapzan, L., Mandorfer, M., Schwarzer, R., Benedikt, S., Viveiros, A., Bauer, D., Ferlitsch, M., Zoller, H., Trauner, M., & Ferlitsch, A. (2020). Anemia and iron deficiency in compensated and decompensated cirrhosis: Prevalence and impact on clinical outcomes. Journal of gastroenterology and hepatology, 35(9), 1619–1627. https://doi.org/10.1111/jgh.14988
8. Bischoff SC, Bernal W, Dasarathy S, Merli M, Plank LD, Schütz T, Plauth M. ESPEN practical guideline: Clinical nutrition in liver disease. Clinical Nutrition. 2020 Dec 1;39(12):3533-62.
9. European Association for The Study of the Liver. EASL Clinical Practice Guidelines for the management of patients with decompensated cirrhosis. Journal of Hepatology. 2018 Aug 1;69(2):406-60.
10. Özatli D, Köksal AŞ, Haznedaroğlu IC, Şimşek H, Karakuş S, Büyükaşik Y, Koşar A, Özcebe O, Dündar S. Anemias in chronic liver diseases. Hematology. 2000 Jan 1;5(1):69-76.
11. Qamar AA, Grace ND, Groszmann RJ, Garcia–Tsao G, Bosch J, Burroughs AK, Ripoll C, Maurer R, Planas R, Escorsell A, Garcia–Pagan JC. Incidence, prevalence, and clinical significance of abnormal hematologic indices in compensated cirrhosis. Clinical Gastroenterology and Hepatology. 2009 Jun 1;7(6):689-95
12. Alexopoulou A, Vasilieva L, Kanellopoulou T, Pouriki S, Soultati A, Dourakis SP. Presence of spur cells as a highly predictive factor of mortality in patients with cirrhosis. Journal of Gastroenterology and Hepatology. 2014 Apr;29(4):830-4.
13. Gkamprela E, Deutsch M, Pectasides D. Iron deficiency anemia in chronic liver disease: etiopathogenesis, diagnosis and treatment. Annals of Gastroenterology. 2017;30(4):405.
14. Hernaez R, Solà E, Moreau R, Ginès P. Acute-on-chronic liver failure: an update. Gut. 2017 Mar 1;66(3):541-53.
15. Girelli D, Pasino M, Goodnough JB, Nemeth E, Guido M, Castagna A, Busti F, Campostrini N, Martinelli N, Vantini I, Corrocher R. Reduced serum hepcidin levels in patients with chronic hepatitis C. Journal of hepatology. 2009 Nov 1;51(5):845-52.
16. Stein J, Connor S, Virgin G, Ong DE, Pereyra L. Anemia and iron deficiency in gastrointestinal and liver conditions. World journal of gastroenterology. 2016 Sep 21;22(35):7908.
17. Ioannou GN, Dominitz JA, Weiss NS, Heagerty PJ, Kowdley KV. The effect of alcohol consumption on the prevalence of iron overload, iron deficiency, and iron deficiency anemia. Gastroenterology. 2004 May 1;126(5):1293-301.
18. Piano S, Tonon M, Vettore E, Stanco M, Pilutti C, Romano A, Mareso S, Gambino C, Brocca A, Sticca A, Fasolato S. Incidence, predictors and outcomes of acute-on-chronic liver failure in outpatients with cirrhosis. Journal of Hepatology. 2017 Dec 1;67(6):1177-84.
19. Anderson ER, Shah YM. Iron homeostasis in the liver. Comprehensive Physiology. 2013 Jan;3(1):315.
20. Yu Y, Jiang L, Wang H, Shen Z, Cheng Q, Zhang P, Wang J, Wu Q, Fang X, Duan L, Wang S. Hepatic transferrin plays a role in systemic iron homeostasis and liver ferroptosis. Blood. 2020 Aug 6;136(6):726-39.
21. Ramm GA, Ruddell RG. Iron homeostasis, hepatocellular injury, and fibrogenesis in hemochromatosis: the role of inflammation in a noninflammatory liver disease. In Seminars in liver disease. 2010 Aug Vol. 30; 271-287. © Thieme Medical Publishers.
22. Jandl JH. The anemia of liver disease: observations on its mechanism. The Journal of Clinical Investigation. 1955 Mar 1;34(3):390-400

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