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Evaluation of the Relationship between Anemia and Liver Disease

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Abstract: Background: Chronic liver conditions are associated with several blood-related disorders. One of these is advanced liver disease, where iron deficiency anemia is often present.

Aim: This study aimed to assess outcomes related to anaemia's effect on patients with liver disease.

Patients and methods: In the achievement of the study's objective, a total of 93 patients' data were collected at different hospitals in Iraq in a period ranged between February 2023 - April 2024. All patients were diagnoses by measurement of HVPG, severity, and others in the laboratory. Our study evaluated mortality rate, Quality - of life, and development of liver disease in related with anemia.

Results: A total of 93 patients had anemia effect on liver disease. The findings shown females had 33.33% and males had of total patients. Fatigue was the most symptom prevalence in the patients, which include 26.88% of patients; the most common cuase was Bleeding, with 44 cases. Severity of anemia is classified into the patients with mild (Hb <12/<13.5 g/dL), include 62 cases; moderate (Hb < 10 g/dL), include 18; severe (Hb < 8 g/dL), include 13. Hepatic venous pressure gradient at patients with liver disease shown HVPG < 10 mm Hg with 19 cases, HVPG ≥ 10-19 mm Hg with 47 cases, and HVPG ≥ 20 mm Hg with 27 cases.

Conclusion: Anemia is a factor that negatively affects patients with liver diseases, severely affecting their general health, quality of life, and performance of daily activities.

Keywords: liver disease; anaemia; Severity of disease; Mortality rate; Quality – life survey.

1. INTRODUCTION

Anemia is a common problem in patients with cirrhosis, with a high prevalence in hospitalized cirrhotics [1 – 5]. The cause of anemia in this population is often multifactorial: chronic

gastrointestinal blood loss due to gastropathy and portal hypertension colopathy, decreased erythrocyte survival, splenic sequestration and hypersplenism, suppression of bone marrow production, deficiency anemias, renal failure and, more rarely, autoimmune hemolytic anemias in relation to some etiologies of cirrhosis are included. [6,7,8,910,11,12]

Despite carrying out the corresponding evaluations, it is difficult to establish the cause of anemia in patients with chronic liver disease because its etiology is multifactorial [13,14,15,16]. The diagnosis of anemia has been established when serum hemoglobin levels are less than 12 g/dl. [18,19,20]

Although anemia is a common complication in hospitalized patients with cirrhosis, there is little information about the prevalence, the factors that may predispose or aggravate this condition, and its importance as a prognostic factor for mortality during hospitalization. [21 – 25]

2. PATIENTS AND METHODS

2.1. Study design

This cross-sectional study included all 93 patients who concurrently had HVPG measures in different hospitals in Iraq. Liver disease (LD) was diagnosed using two non-invasive techniques: transient elastography (TE), which assesses liver stiffness at ≥ 10 kPa, and hepatic venous pressure gradient (HVPG), measured in LD patients with HVPG > 6 mm Hg. In accordance with institutional review board standards, patient characteristics, encompassing clinical and laboratory indicators, were extracted from computerized medical records. The laboratory data were collected on the day of the HVPG measurement or within three months preceding or after the (HVPG) measure. The MELD and Child-Pugh scores were computed.

Anaemia was classified as ‘mild’ if haemoglobin (Hb) concentration fell below the specific to gender lower limit of normal (i.e., under 12 g/dL for females and less than 13.5 g/dL for men) but remained at or above ten g/dL. A 'moderate' grade was designated when hemoglobin fell under ten g/dL but was at least eight g/dL, but I categorized instances as 'severe' anemia when hemoglobin was below eight g/dL. The cut-off values of mean corpuscular volume (MCV) as well as mean corpuscular hemoglobin (MCH) were derived from the reference values provided by the local laboratory.

Thrombocytopenia was identified with a platelet count of <50 G/L, and leukopenia was diagnosed with a white blood cell count at <4 G/L. The likely etiology of anemia was ascertained from centrally archived laboratory test data and/or endoscopic observations (HVPG measurement within a margin of plus or minus three months): Anemia caused by hemorrhage has been identified in instances of normochromic/normocytic anemia when endoscopy or alternative methods revealed signs of acute or chronic bleeding, or in other forms of anemia where endoscopy clearly indicated evidence of hemorrhage.

The identification for hypochromic or microcytic anemias accompanied with authentic iron deficit, as well as diminished serum transferrin and/or ferritin, resulted in the diagnosis of iron-deficiency anemia in this instance. Patients exhibiting hyperchromic and/or macrocytic anemia, as indicated by erythrocyte indices and test findings revealing deficits in vitamin B12 and/or folic acid, were diagnosed as vitamin B12/folate deficiency anemia.

A diagnosis of haemolytic anaemia has been determined in individuals with normochromic or normocytic anemia, decreased haptoglobin levels, or increased unconjugated bilirubin. Nonetheless, people with hypochromic, microcytic anaemia were diagnosed with anemia of chronic illness characterized by elevated ferritin levels.

2.2. A survival rate and mortality rate of patients.

The survival numbers were derived from the patient's data obtained from different hospitals in Iraq. The data, in conjunction with information from medical records, facilitated the differentiation of liver disease-related mortality in other causes of death. We assessed the overall health-related quality of life of patients using the Chronic Liver Condition Questionnaire (CLDQ), which measures the impact of

the condition on patients on a scale of 1 to 7, with higher scores indicating superior health quality of life.

3. RESULTS

TABLE 1. DEMOGRAPIC AND CLINICAL CHARACTERISITCS OF PARTICIPANTS.

Characteristics	Parameters	Participants (n = 93)	Percentage (%)
Age			
	45 – 50	12	12.90%
	51 – 55	15	16.13%
	56 – 60	32	34.41%
	61 – 65	34	36.56%
Sex			
	Males	62	66.67%
	Females	31	33.33%
BMI, Kg/m2			
	Underweight	47	50.54%
	Normal weight	4	4.3%
	Overweight	6	6.45%
	Obese	36	38.71%
Comorbidities			
	Hypertension	24	25.81%
	Diabetes	33	35.48%
	Heart diseases	12	12.90%
	Asthma	8	8.60
	Kidney disease	16	17.20
ASA			
	I	14	15.05%
	II	19	20.43%
	III	25	26.88%
	IV	35	37.63%
Smoking use			
	Yes	37	39.78%
	No	56	60.22%
Alcohol use			
	Yes	7	7.53%
	No	86	92.47%
Education status			
	Primary	29	31.18%
	Secondary	30	32.26%
	Post–graduated university	34	36.56%
Monthly income per dollar			
	< 450	45	48.39%
	451 – 680	33	35.48%
	> 680	15	16.13%

TABLE 2. DISTRIBUTION OF PARTICIPANTS ACCORRDING TO SYMPTOMS.

Symptoms	Participants (n = 93)	Percentage (%)
Fatigue	25	26.88%
Weakness	9	9.68%

Shortness of breath	20	21.51%
Pale skin	10	10.75%
Headaches	14	15.05%
Chest pain	15	16.13%

TABLE 3. DISTRIBUTION OF PARTICIPANTS ACCORRDING TO CAUSES.

Symptoms	Participants (n = 93)	Percentage (%)
Bleeding	44	47.31%
Iron deficiency	17	18.28%
Vitamin B12/folic acid deficiency	12	12.9%
Renal anaemia	13	13.98%
Haemolytic	3	3.23%
Chronic inflammation	4	4.3%

TABLE 4. ENROL OF END-STAGE OF LIVER DISEASE AT PATIENTS.

Variables	Participants (n = 93)	Percentage (%)
Compensated liver disease	46	49.46%
Refractory ascites	13	13.98%
International normalized ratio	1.4 ± 0.2	
Albumin, g/L	35.6 ± 5.5	
Platelet count, G/L	125.8 ± 68.3	
Varices, n (%)	58	62.37%
Haemoglobin levels (g/dL)	13.4 ± 1.7	
G/L: Gigaliters, where it represents a unit which measures the volume that showing a billion liters. In terms of the white blood cell count, the abbreviation G/L signifies the number of white blood cells present in billions per liter of blood.		

TABLE 5: DISTRIBUTION OF PARTICIPANTS ACCORRDING TO SEVERITY OF ANAEMIA.

Scores	**Participants (n = 93)**	**Percentage (%)**
Mild (Hb <12/<13.5 g/dL)	62	66.67%
Moderate (Hb > 8 g/dL)	18	19.35%
Severe (Hb < 8 g/dL)	13	13.98%

Data	**93 Cases**	**Percentage**
Mean corpuscular volume		
Microcytic (<78 fL)	14	15.05%
Normocytic (78-98 fL)	69	74.19%
Macrocytic (>98 fL)	10	10.75%
Mean corpuscular haemoglobin		
Hypochrome (<27 pg)	24	25.81%
Normochrome (27-33 pg)	56	60.22%
Hyperchrome (>33 pg)	13	13.98%

FIGURE 1. ENORLL OF DIAGNOSES DATA IN TERMS OF MEAN CORPUSCULAR VOLUME AND MEAN CORPUSCULAR HAEMOGLOBIN.

TABLE 6. ENROL OF HEPATIC VENOUS PRESSURE GRADIENT AT PATIENTS WITH LIVER DISEASE.

Items	93 Cases	Percentage
HVPG < 10 mm Hg	19	20.43%
> 10 HVPG < 19 mm Hg	47	50.54%
HVPG ≥ 20 mm Hg	27	29.03%

TABLE 7. A QUESTIONNAIRE OF EVALUATION GENERAL HEALTH QUALITY – LIFE AT PATIENTS WITH LIVER DISEASE BY CLDQ SCALE

ITEMS	CLDQ SCALE, Mean ± SD
Abdominal Symptoms	3.2 ± 0.1
Fatigue	3.7 ± 1.2
Systemic Symptoms	2.8 ± 1.1
Daily activity	2.9 ± 0.6
Emotional Function	3.6 ± 0.6
Worry	3.1 ± 0.5

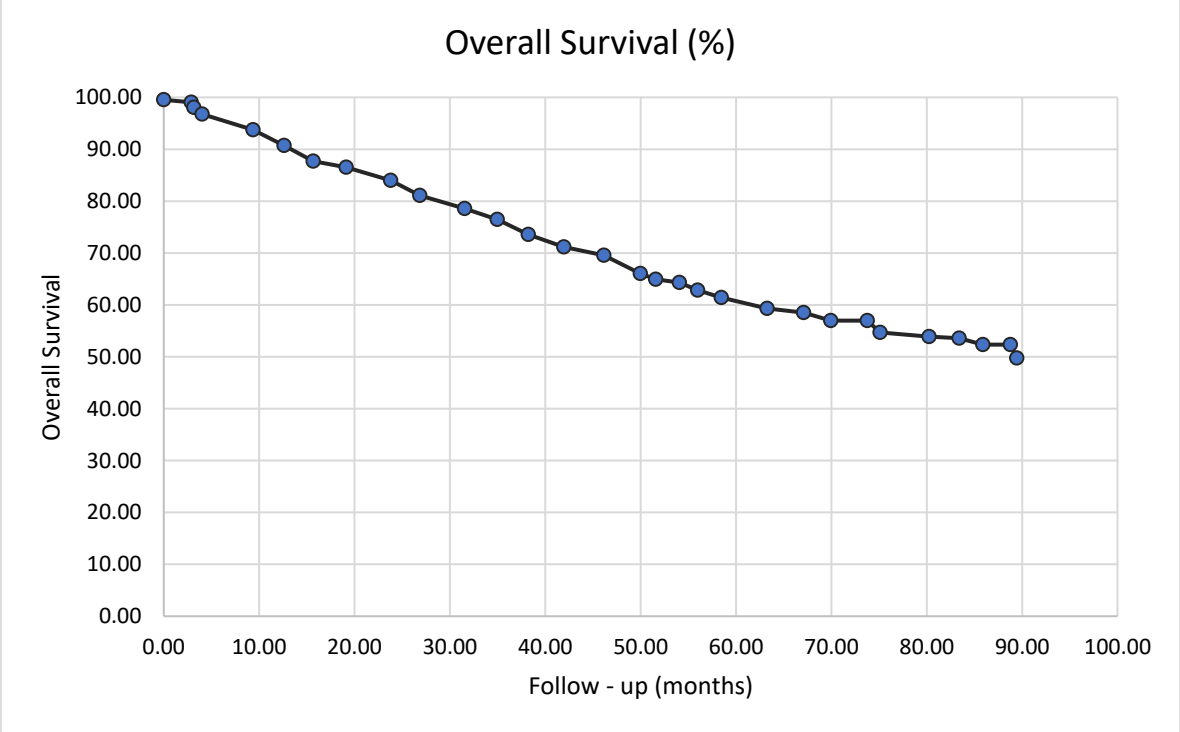

FIGURE 2. OVERALL SURVIVAL RATE OF PATIENTS WITH LIVER DIESESE AFTER ANEMIA AFFECT.

4. DISCUSSION

Chronic illness is common, and more often than not, anemia is present among patients suffering from chronic conditions [26,27,28]. There is increased health burdens associated with poor mental and physical well-being [29], such as dementia and early death. In addition, a proper supply of oxygen is required to ensure normal functioning of all organs especially when a patient is under stress or in critical illness [30,31,32,33]. However, there is scanty information on the extent of the prevalence of anaemia associated with liver disease. In our investigation, the global occurrence of anaemia was also 100%, with 13.98% of the respondents being classified as severely anemic-these findings are consistent with the earlier studies. Anaemia was found to correlate more strongly with indicators of advanced liver disease such as higher MELD and CPS scores as well as severity of portal

hypertension. The above points suggest that anaemia is related to the liver and its complications, portal hypertension, in these patients.

Increased severity of anaemia in CSPH patients has a pathogenic basis, as evidenced by the inverse relationship between the level of haemoglobin and HVPG that has been recommended in a small cohort prior. Moreover, we found that advanced portal hypertension in patients was associated with a higher prevalence of moderatesevere anaemia. The pathogenic mechanisms contributing to anaemia associated with portal hypertension may be related to bleeding from the gastrointestinal tract and the development of hypersplenism-related pancytopenia. [34,35]

Our cohort revealed that patients diagnosed with Alcohol Liver Disease (ALD) had a higher incidence of anemia. In fact, the abuse of alcohol is the predominant reason for the deficiency in vitamin B12 and/or folic acid. Alcohol-related liver disease (ALD) patients suffering from alcohol-associated cirrhosis (ACLD) may moreover experience an exacerbation of anemia due to other etiological factors, and in turn, 81% of patients with alcoholic ACLD are anemic.

It is worthy to note that patients with aetiology of liver disease (LD) were more common among those with advanced portal hypertension. LD was found in 20.43% of patients with HVPG levels of less than ten mmHg, 50.54% in 10-19 mmHg, and 29.03% in patients who had HVPG greater than or equal to 20 mmHg.

It is noteworthy that the presence and degree of anaemia were associated with negative effects [36]. Patients with anaemia had a significantly increased incidence of liver decompensation. Furthermore, anaemic patients had more hospitalizations and had a higher incidence of developing ACLF. [37] The incidence rate of ACLF gradually rose with higher degrees of anemia. Recently, anemia has been identified as a distinct risk indicator in the development of ACLF, including arterial pressure level, the presence of ascites, and MELD score. [39] The elevated rate of hepatic decompensation, as well as ACLF, has contributed to a rise in liver-related mortality and reduced survival rates. [38,39]

5. CONCLUSION

Anemia has a high prevalence with an increase in hospital mortality, although it was not an independent predictor for death risk. There is a correlation between the risk of anaemia and portal hypertension, as well as the degree of liver dysfunction. These anaemia signs can greatly affect a patient's health-related quality of life and daily functioning in the presence of liver disease.

6. REFERENCES

1. Guralnik JM, Eisenstaedt RS, Ferrucci L, Klein HG, Woodman RC. Prevalence of anemia in persons 65 years and older in the United States: evidence for a high rate of unexplained anemia. Blood. 2004;104 (8):2263-2268.
2. Denny SD, Kuchibhatla MN, Cohen HJ. Impact of anemia on mortality, cognition, and function in community-dwelling elderly. Am J Med. 2006;119 (4):327-334.
3. Beghe C, Wilson A, Ershler WB. Prevalence and outcomes of anemia in geriatrics: a systematic review of the literature. Am J Med. 2004;116 (Suppl 7A):3s-10s.
4. Gaskell H, Derry S, Andrew Moore R, McQuay HJ. Prevalence of anaemia in older persons: a systematic review. BMC Geriatr. 2008; 8:1.
5. Weiss G, Goodnough LT. Anemia of chronic disease. N Engl J Med. 2005;352 (10):1011-1023.
6. Terekeci HM, Kucukardali Y, Onem Y, et al. Relationship between anaemia and cognitive functions in elderly people. Eur J Intern Med. 2010;21 (2):87-90.
7. Hong CH, Falvey C, Harris TB, et al. Anemia and risk of dementia in older adults: findings from the health ABC study. Neurology. 2013;81 (6):528-533.

8. Jeong S-M, Shin DW, Lee JE, Hyeon JH, Lee J, Kim S. Anemia is associated with the incidence of dementia: a national health screening study in Korea involving 37,900 persons. Alzheimers Res Ther. 2017; 9:94.
9. Caro JJ, Salas M, Ward A, Goss G. Anemia as an independent prognostic factor for survival in patients with cancer: a systemic, quantitative review. Cancer. 2001;91 (12):2214-2221.
10. Mandorfer M, Payer BA, Scheiner B, et al. Health-related quality of life and severity of fatigue in HIV/HCV co-infected patients before, during, and after antiviral therapy with pegylated interferon plus ribavirin. Liver Int. 2014;34 (1):69-77.
11. Vincent JL, Baron JF, Reinhart K, et al. Anemia and blood transfusion in critically ill patients. JAMA. 2002;288 (12):1499-1507.
12. Maruyama S, Hirayama C, Yamamoto S, et al. red blood cell status in alcoholic and non-alcoholic liver disease. J Lab Clin Med. 2001;138 (5):332-337.
13. Mathurin SA, Aguero AP, Dascani NA, et al. Anemia in hospitalized patients with cirrhosis: prevalence, clinical relevance, and predictive factors. Acta Gastroenterol Latinoam. 2009;39 (2):103-111.
14. Qamar AA, Grace ND, Groszmann RJ, et al. Incidence, prevalence, and clinical significance of abnormal hematologic indices in compensated cirrhosis. Clin Gastroenterol Hepatol. 2009;7 (6):689-695.
15. Kalaitzakis E, Josefsson A, Castedal M, et al. Hepatic encephalopathy is related to anemia and fat-free mass depletion in liver transplant candidates with cirrhosis. Scand J Gastroenterol. 2013;48 (5):577-584. [PubMed] [Google Scholar]
16. Reiberger T, Puspok A, Schoder M, et al. Austrian consensus guidelines on the management and treatment of portal hypertension (Billroth III). Wien Klin Wochenschr. 2017;129 (Suppl 3):135-158.
17. Ripoll C, Garcia-Tsao G. The management of portal hypertensive gastropathy and gastric antral vascular ectasia. Dig Liver Dis. 2011;43 (5):345-351.
18. Luo J-C, Leu H-B, Hou M-C, et al. Cirrhotic patients at increased risk of peptic ulcer bleeding: a nationwide population-based cohort study. Aliment Pharmacol Ther. 2012;36 (6):542-550.
19. Gado A, Ebeid B, Axon A. Prevalence and outcome of peptic ulcer bleeding in patients with liver cirrhosis. Alexandria J Med. 2014;50 (2):143-148.
20. 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. J Gastroenterol Hepatol. 2014;29 (4):830-834.
21. Vassiliadis T, Mpoumponaris A, Vakalopoulou S, et al. Spur cells and spur cell anemia in hospitalized patients with advanced liver disease: Incidence and correlation with disease severity and survival. Hepatol Res. 2010;40 (2):161-170.
22. Lu YF, Li XQ, Han XY, Gong XG, Chang SW. Peripheral blood cell variations in cirrhotic portal hypertension patients with hypersplenism. Asian Pac J Trop Med. 2013;6 (8):663-666.
23. Lv Y, Yee Lau W, Wu H, et al. Causes of peripheral cytopenia in hepatitic cirrhosis and portal hypertensive splenomegaly. Exp Biol Med (Maywood). 2017;242 (7):744-749.
24. Lindenbaum J, Roman MJ. Nutritional anemia in alcoholism. Am J Clin Nutr. 1980;33 (12):2727-2735.
25. Gkamprela E, Deutsch M, Pectasides D. Iron deficiency anemia in chronic liver disease: etiopathogenesis, diagnosis and treatment. Ann Gastroenterol. 2017;30 (4):405-413.

26. Gonzalez-Casas R, Garcia-Buey L, Jones EA, Gisbert JP, Moreno-Otero R. Systematic review: hepatitis-associated aplastic anaemia–a syndrome associated with abnormal immunological function. Aliment Pharmacol Ther. 2009;30 (5):436-443.
27. Kalaitzakis E, Josefsson A, Castedal M, et al. Factors related to fatigue in patients with cirrhosis before and after liver transplantation. Clin Gastroenterol Hepatol. 2012;10 (2):174-181, 81.e1.
28. Les I, Doval E, Flavià M, et al. Quality of life in cirrhosis is related to potentially treatable factors. Eur J Gastro Hepatol. 2010;22 (2):221-227.
29. Gungor G, Akyildiz M, Keskin M, et al. Is there any potential or additive effect of anemia on hepatorenal syndrome? Turkish J Gastroenterol. 2016;27 (3):273-278.
30. de Franchis R, Baveno V. Expanding consensus in portal hypertension: Report of the Baveno VI Consensus Workshop: stratifying risk and individualizing care for portal hypertension. J Hepatol. 2015;63 (3):743-752.
31. McClellan W, Aronoff SL, Bolton WK, et al. The prevalence of anemia in patients with chronic kidney disease. Curr Med Res Opin. 2004;20 (9):1501-1510.
32. Ferlitsch A, Bota S, Paternostro R, et al. Evaluation of a new balloon occlusion catheter specifically designed for measurement of the hepatic venous pressure gradient. Liver Int. 2015;35 (9):2115-2120.
33. Reiberger T, Ferlitsch A, Payer BA, et al. Non-selective beta-blockers improve the correlation of liver stiffness and portal pressure in advanced cirrhosis. J Gastroenterol. 2012;47 (5):561-568.
34. Reiberger T, Ferlitsch A, Payer BA, et al. Noninvasive screening for liver fibrosis and portal hypertension by transient elastography—a large single-center experience. Wien Klin Wochenschr. 2012;124 (11):395-402.
35. Schwabl P, Bota S, Salzl P, et al. new reliability criteria for transient elastography increase the number of accurate measurements for screening of cirrhosis and portal hypertension. Liver Int. 2015;35 (2):381-390.
36. Margini C, Murgia G, Stirnimann G, et al. Prognostic significance of controlled attenuation parameter in patients with compensated advanced chronic liver disease. Hepatol Commun. 2018;2 (8):929-940.
37. Abraldes JG, Bureau C, Stefanescu H, et al. Noninvasive tools and risk of clinically significant portal hypertension and varices in compensated cirrhosis: the "Anticipate" study. *Hepatology*. 2016;64 (6):2173-2184.
38. Hernaez R, Sola E, Moreau R, Gines P. Acute-on-chronic liver failure: an update. *Gut*. 2017;66 (3):541-553.
39. Scheiner B, Steininger L, Semmler G, et al. Controlled attenuation parameter does not predict hepatic decompensation in patients with advanced chronic liver disease. *Liver Int*. 2019;39 (1):127-135.