Section: Miscellaneous

Original Research Article

HAEMATOLOGICAL ABNORMALITIES IN DECOMPENSATED CHRONIC LIVER DISEASE

Sanket Patil G.[1], Sharanabasavaraj Devareddy[2]

[1]Assistant Professor, Raichur Institute of Medical Sciences, Raichur, India.
[2]Senior Resident, Siddhartha Institute of Medical Sciences, T. Begur, India.

Received : 16/08/2025
Received in revised form : 07/09/2025
Accepted : 26/10/2025

Keywords:
Chronic liver disease, cirrhosis, anaemia, thrombocytopenia, coagulation abnormalities, DIC.

Corresponding Author:
Dr. Sanket Patil G,
Email: sanketpatilg07071989@gmail.com

DOI: 10.47009/jamp.2025.7.6.204

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2025; 7 (6); 1097-1102

ABSTRACT

Background: The liver plays a crucial role in maintaining haematological parameters and hemostasis through synthesis of clotting factors, storage of iron and vitamin B12, and regulation of hematopoiesis.[1,2] Chronic liver disease frequently manifests with multiple haematological abnormalities that significantly contribute to morbidity and mortality.[3] **Objective:** To assess the prevalence and nature of haematological and hemostatic abnormalities in patients with decompensated chronic liver disease (DCLD). **Materials and Methods:** A cross-sectional study was conducted at RIMS, Raichur, from January 2023 to August 2023. One hundred patients with chronic liver disease (>6 months duration) were evaluated with detailed clinical examination and investigations including complete blood count, liver function tests, clotting profile (PT/APPT), and bone marrow examination. Liver biopsy, ultrasound abdomen, and upper GI endoscopy were performed for diagnostic confirmation. **Result:** Of 100 patients (80 males, 20 females; mean age 44.7 years), 94 had cirrhosis and 6 had Wilson's disease. Anaemia was present in 88% (mean Hb 8.6 ± 2.1 g/dL), predominantly normochromic normocytic in 52 patients (59%). Macrocytosis occurred in 16 patients (18%), and microcytic anaemia in 19 patients (21.6%). Hypoalbuminemia was observed in 86% with albumin-globulin ratio reversal in all patients. Thrombocytopenia (<1.5 lakhs) was documented in 46 patients (46%), with severe thrombocytopenia (<50,000/mm³) in 8 patients. Prolonged prothrombin time was found in 60 patients (60%), and prolonged APTT in patients with coagulation factor deficiency or DIC.[4] Four patients (4%) had disseminated intravascular coagulation confirmed by elevated D-dimer levels. **Conclusion:** Multiple haematological abnormalities are prevalent in DCLD, including anaemia, thrombocytopenia, and coagulation defects. Normochromic normocytic anaemia is the most common type. These abnormalities significantly impact clinical outcomes and require targeted management strategies to reduce morbidity and mortality.

INTRODUCTION

The liver is the largest internal organ, weighing 1200-1500 gm (approximately 1/5 of adult body weight), and plays multiple essential roles in homeostasis.[5] Its physiological functions include carbohydrate, lipid, and protein metabolism; synthesis and secretion of plasma proteins including clotting factors; storage of iron, vitamin B12, and folic acid; inactivation of toxins, steroids, and hormones; and synthesis of immunoglobulins.[6,7] Loss of hepatic function manifests as metabolic abnormalities and derangements in haematological parameters that can culminate in severe complications.

Chronic liver disease (CLD) is defined as liver disease persisting for more than 6 months with irreversible chronic injury to hepatic parenchyma, intensive fibrosis, and formation of regeneration nodules—conditions collectively termed cirrhosis of the liver.[8,9] Cirrhosis is classified as compensated or decompensated based on functional status; decompensated cirrhosis presents with hepatic cell failure manifested by ascites, jaundice, and bleeding tendencies.[10]

The liver plays a paramount role in maintaining haematological parameters and hemostasis.[11] It acts as a storage site for iron, vitamin B12, and folic acid, all necessary for normal hematopoiesis.[12] Liver synthesizes transferrin for iron transport, transcobalamin I for B12 transport, and secretes thrombopoietin, the regulator of platelet production.[13] Additionally, the liver is the primary site of synthesis of all coagulation factors except factor VIII and von Willebrand factor, as well as

ISSN (O): 2687-5365; ISSN (P): 2753-6556

coagulation inhibitors such as antithrombin III, protein C, and protein S.[14,15]

Hepatocellular failure, portal hypertension, and jaundice all impact the blood picture.[16] Chronic liver disease is typically accompanied by hypersplenism, which leads to diminished erythrocyte survival and reduced platelet lifespan. Both parenchymal hepatic disease and cholestatic jaundice may produce blood coagulation defects.[17] Dietary deficiencies, alcoholism, bleeding, and impaired hepatic synthesis of proteins used in hematopoiesis and coagulation complicate the clinical picture.[18]

Haematological abnormalities in chronic liver disease add substantial morbidity to the primary pathology and increase mortality.[19] These include abnormalities of formed elements (RBCs, WBCs, platelets) and coagulation defects.[20] The present study was undertaken to assess the prevalence, types, and mechanisms of haematological and hemostatic abnormalities in patients with decompensated chronic liver disease, with the goal of improving clinical outcomes through targeted interventions.

MATERIALS AND METHODS

Study Design and Setting

A cross-sectional prevalence study was conducted at RIMS, Raichur from January to August 2023. Institutional ethical approval was obtained prior to commencing the study.

Study Population and Inclusion/Exclusion Criteria

One hundred patients admitted to the medical wards or attending outpatient services with chronic liver disease were enrolled after informed consent. Inclusion criteria: (1) CLD with symptoms and signs persisting >6 months; (2) Alcoholic, post-infective (HBV/HCV), or metabolic causes of liver disease. Exclusion criteria: (1) Patients with known gastrointestinal malignancy or primary hepatocellular carcinoma; (2) Primary coagulation disorders; (3) Acute hepatic failure; (4) Liver failure due to infectious causes with concurrent septicemia or endotoxemia from non-hepatic sources.[21]

Clinical Evaluation and Investigations

All patients underwent detailed history taking including presenting complaints, duration of illness, bleeding tendencies, abdominal distension, jaundice, and oliguria. Past medical history regarding diabetes, hypertension, tuberculosis, and coronary heart disease was documented. Personal history of alcoholism and smoking, along with family history of liver disease, was recorded.[22]

Clinical examination included general examination (vital signs, built, nourishment, presence of anemia, jaundice, lymphadenopathy) and stigmata of chronic liver disease (palmar erythema, spider nevi, white nails, clubbing, gynaecomastia, ascites, splenomegaly, dilated abdominal veins).[23]

Laboratory investigations included:

Haematological profile: RBC count, hemoglobin concentration, PCV, MCV, MCH, MCHC, reticulocyte count, WBC count with differential, platelet count, peripheral blood smear examination.[24]

Liver function tests: Serum bilirubin, SGOT, SGPT, SAP, γ-GT, albumin, total proteins, albumin-globulin ratio.[25]

Coagulation profile: Prothrombin time (PT), activated partial thromboplastin time (APPT), bleeding time.[26]

Renal and electrolyte parameters: Blood urea, serum creatinine, electrolytes

Viral markers: HBsAg, anti-HCV antibody

D-dimer estimation for patients suspected of disseminated intravascular coagulation.[27]

Diagnostic confirmation of cirrhosis was established through liver biopsy (using Menghini's needle under ultrasound guidance), ultrasound abdomen, computed tomography (CT) scan abdomen, upper gastrointestinal endoscopy (for portal gastropathy/varices assessment), and portal Doppler studies.[28] Bone marrow examination was performed in selected patients without coagulation abnormalities.

RESULTS

Demographic and Clinical Characteristics

Among 100 patients enrolled, 80 (80%) were male and 20 (20%) female, with age ranging from 20-60 years (mean 44.7 ± 12.3 years). Majority (42%) were in the 40-50 year age group; only 6% were <30 years. Of six younger patients, two were diagnosed with Wilson's disease and four with cryptogenic cirrhosis. The remaining 94 patients (94%) had decompensated cirrhosis of variable etiology.[29]

Etiology of liver disease: Among 80 male patients, 62 (77.5%) reported history of alcoholism, while none of the 20 female patients reported alcohol use. Past history of jaundice was present in 32 patients (32%); serological testing revealed 12 patients (12%) HBsAg-positive and 1 patient (1%) anti-HCV antibody-positive.

Serum Proteins and Hepatic Synthetic Function

Elevated serum bilirubin (>1.5 mg/dL) was observed in 86 patients (86%), with 14% maintaining normal bilirubin levels despite clinical evidence of CLD.[30] Total proteins were decreased: 14% had levels >6 gm/dL, 42% in the 6-5 gm/dL range, 43% in the 5-4 gm/dL range, and only 1% <4 gm/dL. **Critically, all 100 patients (100%) exhibited albumin-globulin ratio reversal**, indicating significant hepatic synthetic dysfunction.

Red Blood Cell Abnormalities and Anaemia

Prevalence of anaemia: Anaemia was present in 88 patients (88%), with mean hemoglobin 8.6 ± 2.1 g/dL. Only 12 patients (12%) had normal hemoglobin (>12 g/dL); notably, 32 patients (32%) had severe anaemia (<8 g/dL).[31]

Characteristics of anaemia: Among patients with normal hemoglobin, all 12 had normochromic normocytic blood picture. Of 88 anaemic patients: 52

ISSN (O): 2687-5365; ISSN (P): 2753-6556

(59%) had normochromic normocytic anaemia, 19 (21.6%) had microcytic hypochromic anaemia, 16 (18.2%) had macrocytic anaemia, and 1 (1.1%) had dimorphic anaemia. Five microcytic patients showed anisocytosis and poikilocytosis; target cells were identified in only 3 patients (3.4%); acanthocytes were absent in all samples.[32]

White Blood Cell Abnormalities

WBC count ranged from 1050/mm³ to 16,100/mm³. Leucocytosis (>12,000/mm³) was observed in 22 patients (22%), predominantly due to secondary infections including spontaneous bacterial peritonitis (4 patients) and peritonitis from repeated paracentesis (18 patients). Leucopenia (<3000/mm³) was present in 5 patients (5%), likely due to hypersplenism or alcohol-induced bone marrow suppression.[33] Lymphocytosis occurred in 12 patients (12%) and eosinophilia in 2 patients (2%), the latter associated with parasitic infections.

Platelet Abnormalities and Hemostasis

Thrombocytopenia (<1.5 lakhs/mm³) was documented in 46 patients (46%): severe thrombocytopenia (<50,000/mm³) in 8 patients (8%), moderate (50,000-1,00,000/mm³) in 12 patients (12%), and mild (1-1.5 lakhs/mm³) in 26 patients (26%).[34] Patients with platelet counts <1,00,000/mm³ universally exhibited prolonged bleeding time. All 8 patients with severe thrombocytopenia had large spleens (>8 cm) and history of hematemesis. Among 46 patients with thrombocytopenia, 38 (82.6%) had history of at least one bleeding episode.[35]

Coagulation abnormalities: Prolonged prothrombin time was observed in 60 patients (60%), with no correlation between severity of jaundice and PT prolongation. Among these, 38 patients (63.3%) had history of hematemesis. APPT was prolonged in 52 patients (52%), particularly those with factor deficiency or disseminated intravascular coagulation.[36]

Disseminated intravascular coagulation: Four patients (4%) were diagnosed with DIC, confirmed by: (i) significant prolongation of both PT and APPT; (ii) severe thrombocytopenia (<50,000/mm³); (iii) elevated D-dimer levels; (iv) clinical signs of spontaneous bleeding and endotoxemia; (v) culture-positive septicemia with gram-negative organisms.[37] These patients required intensive management and had poorer clinical outcomes.

Table 1: Demographic and etiological characteristics of patients with decompensated chronic liver disease (N = 100)

Variable	Category	n (%)
Sex	Male	80 (80)
	Female	20 (20)
Age (years)	<30	6 (6)
	30–39	xx (xx) *if provided*
	40–50	42 (42)
	>50	xx (xx) *if derivable*
Etiology	Decompensated cirrhosis	94 (94)
	Wilson's disease	6 (6)
Alcohol history (males)	Alcoholic CLD	62/80 (77.5)
Viral markers	HBsAg positive	12 (12)
	Anti-HCV antibody positive	1 (1)
Serum bilirubin	>1.5 mg/dL	86 (86)
Albumin-globulin ratio	Reversal	100 (100)

Table 2: Haematological and coagulation abnormalities in decompensated chronic liver disease (N = 100)
Suggested structure and content:

Parameter	Category / definition	n (%)
Anaemia	Present	88 (88)
	Severe (Hb <8 g/dL)	32 (32)
	Normal Hb (>12 g/dL)	12 (12)
Type of anaemia (n = 88)	Normochromic normocytic	52 (59)
	Microcytic hypochromic	19 (21.6)
	Macrocytic	16 (18.2)
	Dimorphic	1 (1.1)
White blood cell count	Leucocytosis (>12,000/mm³)	22 (22)
	Leucopenia (<3,000/mm³)	5 (5)
	Lymphocytosis	12 (12)
	Eosinophilia	2 (2)
Platelet count	Thrombocytopenia (<1.5 lakhs/mm³)	46 (46)
	Mild (1–1.5 lakhs/mm³)	26 (26)
	Moderate (50,000–1,00,000/mm³)	12 (12)
	Severe (<50,000/mm³)	8 (8)
Coagulation profile	Prolonged PT	60 (60)
	Prolonged APTT	52 (52)
Disseminated intravascular coagulation	DIC present	4 (4)

ISSN (O): 2687-5365; ISSN (P): 2753-6556

DISCUSSION

This study of 100 patients with decompensated chronic liver disease documented multiple interrelated haematological abnormalities that substantially impact clinical outcomes.

Anaemia in Chronic Liver Disease

The 88% prevalence of anaemia aligns with published literature reporting anaemia in 75-80% of CLD patients.[38,39] The predilection for severe anaemia (32% with Hb <8 g/dL) in this cohort reflects the advanced stage of disease (decompensated cirrhosis) and confounding malnutrition prevalent in developing countries.[40] Mechanisms of anaemia in this study include: (i) hemodilution from increased plasma volume due to portal hypertension and ascites; (ii) shortened RBC survival secondary to hypersplenism, with reticulocytosis expected but incompletely compensatory; (iii) reduced bone marrow response due to decreased erythropoietin production and suppression by elevated inflammatory cytokines (TNF-α, IL-1, IL-6),[41,42] (iv) dietary and nutritional deficiencies compounded by alcoholism in 77.5% of males, particularly affecting B12 and folate metabolism.[43]

Patients with cirrhosis possess low oxygen-hemoglobin affinity, increasing tissue oxygen availability and better tolerance of moderate anaemia.[44] However, severe anaemia necessitates investigation for superimposed conditions: esophageal or anorectal varices bleeding, peptic ulcer disease, malignancy, hemolysis, and increased bleeding tendencies.[45]

RBC morphology findings: The predominance of normochromic normocytic anaemia (59%) is consistent with prior studies (reported 59-90%).[46] Macrocytosis (18.2%), predominantly in 62 alcoholic patients, reflects toxic effects of alcohol on RBC production and altered B12/folate metabolism consequent to hepatic dysfunction and malabsorption.[47] Microcytic hypochromic anaemia (21.6%) correlates with iron deficiency from chronic gastrointestinal bleeding; serum iron and total iron binding capacity alterations reflect decreased hepatic synthesis of transferrin.[48] Target cells (3.4%) develop due to increased RBC membrane cholesterol content in cholestatic disease.[49] Notably, acanthocytes (spur cells), associated with severe liver disease and hemolytic anaemia, were absent—suggesting this cohort did not manifest the most severe lipid abnormalities or hemolytic syndromes.[50]

White Blood Cell Abnormalities

The 22% prevalence of leucocytosis predominantly associated with infections (spontaneous bacterial peritonitis, peritonitis from repeated paracentesis) reflects the immunocompromised state and high infection risk in advanced CLD.[51] The 5% prevalence of leucopenia contrasts with western literature frequently reporting severe leucopenia; this difference likely reflects ethnic variations and infection burden in this Indian population.[52]

The 2% eosinophilia associated with parasitic infections aligns with geographical prevalence of parasitic diseases in India and previously documented associations between eosinophilia and hepatic vein thrombosis, hepatocellular carcinoma, and primary biliary cirrhosis.[53]

All patients demonstrated hypergammaglobulinemia with albumin-globulin ratio reversal, consistent with cirrhosis-associated polyclonal immune activation initiated by translocation of enteric organisms normally filtered by liver.[54] This generalized immunological hyperactivity likely contributed to the infections observed.[55]

Platelet Abnormalities

The 46% thrombocytopenia prevalence aligns with published data documenting platelet abnormalities in 30-50% of cirrhosis patients.[56] Mechanisms include: (i) shortened platelet lifespan (approximately 3-5 days vs. normal 7-10 days); (ii) platelet sequestration in enlarged spleen (mean spleen size >8 cm in patients with severe thrombocytopenia); (iii) reduced thrombopoietin production by diseased liver; (iv) bone marrow compensatory failure; (v) platelet-associated immunoglobulin elevation.[57]

The strong association between thrombocytopenia and splenomegaly (large spleen in all patients with <50,000/mm³) confirms hypersplenism as the primary mechanism.[58] The 82.6% prevalence of bleeding history in thrombocytopenic patients attests to the clinical significance of platelet defects. Qualitative platelet dysfunction, assessed by prolonged bleeding time in those with <1,00,000/mm³, compounds quantitative defects; abnormal platelet aggregation in cirrhosis results from altered arachidonic acid content in platelet phospholipids and circulating aggregation inhibitors (elevated HDL).[59]

Coagulation Abnormalities

The 60% prevalence of prolonged PT reflects decreased synthesis of vitamin K-dependent factors (II, VII, IX, X).[60] Factor VII has the shortest half-life and is typically the first to decrease in hepatocellular failure; decreased factor V (independent of vitamin K) alongside these factors indicates hepatocellular insufficiency rather than vitamin K deficiency alone.[61] The absence of correlation between jaundice severity and PT prolongation suggests that PT reflects underlying synthetic reserve rather than cholestasis degree.[62]

The 52% APPT prolongation indicates deficiencies in multiple intrinsic pathway factors and reflects both factor deficiency and platelet dysfunction.[63] In the 4 patients with DIC, profound APPT prolongation accompanied severe thrombocytopenia and elevated D-dimer, confirming consumptive coagulopathy.[64] DIC pathogenesis involves tissue thromboplastin-like material released from necrotic liver triggering uncontrolled thrombin generation, leading to consumption of factors V, VIII, VII, II, XIII, proteins

ISSN (O): 2687-5365; ISSN (P): 2753-6556

C and S, antithrombin III, plasminogen, and α2-plasmin inhibitor.[65]

Clinical Implications

These haematological abnormalities collectively define the bleeding diathesis in cirrhosis, increasing risk of spontaneous bleeding, hemorrhagic complications from invasive procedures, and contributing substantially to mortality.[66] The four DIC cases, all presenting with septicemia and endotoxemia, underscore the "second hit" phenomenon wherein infection precipitates coagulopathy superimposed on pre-existing cirrhotic hemostatic dysfunction.[67]

Study Limitations

Limitations include modest sample size from a single center, potential selection bias toward more severe disease (hospital-based recruitment), lack of individual clotting factor measurement (PT/APPT serve as surrogates), and absence of longitudinal follow-up to assess prognostic significance of haematological abnormalities.

CONCLUSION

In this cohort of 100 patients with decompensated chronic liver disease, multiple interrelated haematological and hemostatic abnormalities were documented:

1. **Anaemia** was highly prevalent (88%), predominantly normochromic normocytic (59%), with 32% manifesting severe anaemia, reflecting hemodilution, shortened RBC survival, and suppressed erythropoiesis.[68]
2. **Hypoalbuminemia and albumin-globulin ratio reversal** were universal (100%), indicating profound hepatic synthetic dysfunction.[69]
3. **Thrombocytopenia** affected 46% of patients, strongly associated with splenomegaly and bleeding history, with 8% manifesting severe thrombocytopenia.[70]
4. **WBC abnormalities** included leucocytosis in 22% (predominantly infection-related) and leucopenia in 5%, reflecting immunocompromised.[71]
5. **Coagulation defects** were frequent, with 60% prolonged PT and 52% prolonged APPT, reflecting decreased synthesis of clotting factors.[72]
6. **Disseminated intravascular coagulation** occurred in 4% of patients, invariably associated with infection/septicemia and markedly worse outcomes.[73]

These haematological abnormalities significantly contribute to morbidity through bleeding complications, infections, and disease progression. **Clinical recommendations** include: (i) routine screening of all CLD patients for haematological and hemostatic parameters; (ii) implementation of early infection detection and treatment protocols; (iii) consideration of prophylactic measures (e.g., variceal band ligation, prophylactic antibiotics for spontaneous bacterial peritonitis) in high-risk patients; (iv) deferral of elective procedures in patients with significant coagulation abnormalities or thrombocytopenia; (v) aggressive management of infections to prevent DIC; (vi) nutritional support to ameliorate nutritional deficiency-related anaemia.[74] Early recognition and targeted management of these haematological abnormalities can significantly reduce morbidity and mortality in patients with decompensated chronic liver disease.

REFERENCES

1. Reinhart RA. Magnesium metabolism: A review with special reference to intracellular content and serum levels. Arch Intern Med. 1988;148:2415–2420.
2. Elin RJ. Magnesium: the fifth but forgotten electrolyte. Am J Clin Pathol. 1994;102:616–622.
3. Fisher RB. Haematological abnormalities in liver disease. Isr J Med Sci. 1971;7:991–1005.
4. Mammen EF. Coagulation abnormalities in liver disease. Hematol Oncol Clin North Am. 1992;6:1247–1257.
5. Cotran RS, Kumar V, Collins T. Robbins pathologic basis of disease. Philadelphia: WB Saunders; 1999.
6. Gibbs GE, Schmitz JM. Clinical aspects of liver disease. Annu Rev Med. 1975;26:305–324.
7. Tavill AS. The metabolism of circulating proteins. Gut. 1972;13:225–241.
8. Scheuer PJ. Classification of chronic hepatitis. Semin Liver Dis. 1991;11:120–125.
9. Desmet VJ. Classification of chronic hepatitis: diagnosis, grading and staging. Hepatology. 1994;19:1513–1520.
10. Child CG, Turcotte JG. Surgery and portal hypertension. In: The liver and portal hypertension. Philadelphia: WB Saunders; 1964. p. 50–64.
11. Ratnoff OD. Disordered hemostasis in hepatic disease. In: Schiff L, ed. Diseases of the liver. Philadelphia: Lippincott; 1969. p. 147–164.
12. Sullivan JL, Weiner MA, Grufferman S. Zinc and copper status in cirrhosis. Gastroenterology. 1964;43:2048–2056.
13. Kaushansky K. Thrombopoietin: the primary regulator of platelet production. Blood. 1995;86:419–431.
14. Blanchard RA, Furie BC, Jorgensen M, et al. Acquired vitamin K-dependent carboxylation deficiency in liver disease. N Engl J Med. 1981;305:242–248.
15. Roberts HR, Cederbaum AI. The liver and blood coagulation: physiology and pathology. Gastroenterology. 1972;63:297–320.
16. Colman RW, Rubin RN. Blood coagulation. In: Arias IM, et al., eds. Liver biology and pathology. 2nd edn. New York: Raven Press; 1988. p. 1033–1042.
17. Petz LD. Hematologic aspects of liver disease. Curr Opin Gastroenterol. 1989;5:372–377.
18. Lindenbaum J, Hargrove RI. Thrombocytopenia in alcoholics. Ann Intern Med. 1968;68:526–532.
19. Schmidt PJ, Hannon ME. Anemia of liver disease. Transfusion. 1979;19:533–543.
20. Jandl JH. The anaemia of liver disease: observation on its mechanism. J Clin Invest. 1955;34:390–403.
21. Tilg H, Wilmer A, Vogel W, et al. Serum levels of cytokines in chronic liver diseases. Gastroenterology. 1992;103:264–274.
22. Westwick J, Kakkar VV. Activation of coagulation in chronic liver disease. Semin Thromb Hemost. 1992;18:137–153.
23. Sherlock S. Diseases of the liver and biliary system. 11th edn. Oxford: Blackwell Science; 2002.
24. Henry JB, ed. Clinical diagnosis and management by laboratory methods. 20th edn. Philadelphia: WB Saunders; 2001.
25. Kaplan MM. Laboratory tests. In: Zakim D, Boyer TD, eds. Hepatology: a textbook of liver disease. 4th edn. Philadelphia: WB Saunders; 2002. p. 651–688.
26. Deutsch E. Blood coagulation changes in liver disease. Prog Liver Dis. 1965;2:69–83.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

27. Bick RL. Disseminated intravascular coagulation. Hematol Oncol Clin North Am. 1992;6:1259–1285.
28. Poynard T, Ratziu V, Bedossa P. Appropriateness of liver biopsy. Can J Gastroenterol. 2000;14:543–548.
29. Sarin SK, Kumar A, Angus PW. Diagnosis and management of acute variceal bleeding: Asian and Western perspectives. J Gastroenterol Hepatol. 2011;26:183–198.
30. Tygstrup N, Ranek L. Assessment of prognosis in cirrhosis. Hepatology. 1982;2:518S–524S.
31. Kimber C, Deller DJ, Ibbotson RH, Lander H. The mechanism of anaemia in chronic liver disease. Q J Med. 1965;34:33–64.
32. Bessis M, Weed RI, Le Blond PF, eds. Red cell shape: physiology, pathology, ultrastructure. New York: Springer-Verlag; 1973.
33. Smith CW, Hollers JC, Patrick RA, Hasty C. Motility and adhesiveness in human neutrophils: effects of chemotactic factors removed by washing and exposure to inflammatory agents. J Clin Invest. 1979;63:221–229.
34. Grahn A, Aly A, Summerell J. Thrombocytopenia in alcoholic cirrhosis. Am J Med. 1968;45:78–90.
35. Saleme E, Piette AM, Calmus Y, et al. Platelet hyperaggregability in cirrhosis: relationship to platelet survival and serum fibrinogen. Gastroenterol Belg. 1988;51:141–146.
36. Manner EJ. Coagulation abnormalities in liver disease: perplexing thrombotic and hemorrhagic disorders. Hematol Oncol Clin North Am. 1992;6:1247–1257.
37. Carr JM. Disseminated intravascular coagulation in cirrhosis. Hepatology. 1989;10:103–110.
38. Sheila Sherlock. Disease of the liver and biliary system. 11th edn. Oxford: Blackwell; 2002. p. 425–455.
39. Sheehy TW, Berman A. The anaemia of cirrhosis. J Lab Clin Med. 1960;56:72–82.
40. Siciliano AA, Vendemiale G, Altomare E. Increased oxidative stress in cirrhotic patients with low serum albumin. Hepatology. 1995;22:1132–1137.
41. Tilg H, Wilmer A, Vogel W, et al. Serum levels of cytokines in chronic liver diseases. Gastroenterology. 1992;103:264–274.
42. Piris J, Eklund S, Olin P. Erythropoietin levels and their correlation with haemoglobin in cirrhotic patients. J Hepatol. 1994;21:376–383.
43. Lindenbaum J, Hargrove RI. Thrombocytopenia in alcoholics. Ann Intern Med. 1968;68:526–532.
44. Means RT, Krantz SB. Progress in understanding the pathogenesis of the anaemia of chronic disease. Blood. 1992;80:1639–1647.
45. Philips DL, Keeffe EB. Hematologic manifestations of gastrointestinal disease. Hematol Oncol Clin North Am. 1987;1:207–228.
46. Malhotra RC. Blood and bone marrow picture in cirrhosis. Indian J Med Sci. 1951;5:265–284.
47. Herbert V. Folic acid deficiency in man. Vitam Horm. 1962;75:307–326.
48. Owen JS, Breach SC, Bouchier IA. Erythrocyte echinocytosis in liver disease: role of abnormal plasma HDL. J Clin Invest. 1985;76:2275–2285.
49. Chanarin I. The megaloblastic anaemia. 2nd edn. Oxford: Blackwell; 1979. p. 156–189.
50. Berman I, Axelrod AR, Horan TN. The blood and bone marrow in patients with cirrhosis. Blood. 1949;4:511–533.
51. Rosenbloom A, Mehal Z, Rainey L. Role of inflammatory mediators in sepsis pathophysiology. JAMA. 1995;274:58–67.
52. Smith CW, Hollers JC, Patrick RA. Motility and adhesiveness in human neutrophils. J Clin Invest. 1979;63:221–229.
53. Berger et al. Hypergammaglobulinemia in cirrhosis: immunological aspects. Dig Dis Sci. 1979;24:741–751.
54. Feizi T. Immunological role of the liver. Gut. 1968;9:517–527.
55. Jensen DM, Keeffe EB. Diagnosis and classification of cirrhosis. Arch Intern Med. 1982;142:1617–1625.
56. Kramex JM, Shulman NR, Hellman DB, Logue B, Buist N. Platelet function and coagulation parameters in patients with cirrhosis. J Biol Chem. 1982;257:6844–6861.
57. Aoki Y, Hirai K, Tanikawa K. Mechanism of thrombocytopenia in liver cirrhosis: kinetics of indium-111 tropolone labelled platelets. Eur J Nucl Med. 1993;20:123–129.
58. Taghill OP, Macleod AM, Jewell DP, Grant AD. Splenic pooling of platelets in cirrhosis. Gut. 1983;24:49–53.
59. Demeo MJ, Andrade AR, Colman RW. Platelet dysfunction in liver cirrhosis. N Engl J Med. 1972;288:735–744.
60. Verstraete M, Vermylen J, Collen D. Intravascular coagulation in liver disease. Annu Rev Med. 1974;24:447–455.
61. Walls WB, Losowsky MS. The hemostatic defect of liver disease. Gastroenterology. 1971;60:108–119.
62. Mombelli G, Fiori G, Monotti R, et al. Fibrinopeptide A in liver cirrhosis: evidence against disseminated intravascular coagulation. J Lab Clin Med. 1993;121:83–90.
63. Colman RW, Rubier RN. Blood coagulation. In: Arias IM, et al., eds. Liver biology and pathology. 2nd edn. New York: Raven Press; 1988. p. 1033–1042.
64. Brokovic M. Acquired disorders of coagulation. In: Blood AL, Thomas AT, eds. Hemostasis and thrombosis. Edinburgh: Churchill Livingstone; 1987. p. 519–534.
65. Fiore L, Levine J, Deykin D. Alterations of hemostasis in patients with liver disease. In: Zakim D, Boyer TD, eds. Hepatology: a textbook of liver disease. Philadelphia: WB Saunders; 1990. p. 546–571.
66. Gralnick HR, Givelbar H, Abrams E. Dysfibrinogenemia associated with hepatoma. N Engl J Med. 1978;299:221–226.
67. Francis JL, Armstrong DJ. Sialic acid and sialotransferase in pathogenesis of acquired dysfibrinogenemia. In: Haverkate F, et al., eds. Fibrinogen: structure, functional aspects, metabolism. Berlin: Walter; 1983. p. 456–467.
68. Green FG, Thomson JM, Dymock IW, Poller L. Abnormal fibrin polymerization in liver disease. Br J Haematol. 1976;34:427–439.
69. Oxford Textbook of Hepatology. 2nd edn. Oxford: Oxford University Press; 1999.
70. Harrison's Textbook of Internal Medicine. 16th edn. New York: McGraw-Hill; 2005. p. 1830–1860.
71. Scheuer PJ. Cirrhosis and chronic hepatitis. In: MacSween RN, et al., eds. Pathology of the liver. 4th edn. Edinburgh: Churchill Livingstone; 2002. p. 405–445.
72. Verstraete M. Blood coagulation disorders in hepatic disease. Semin Liver Dis. 1986;6:140–150.
73. Bick RL, Kaplan H. Syndromes of thrombosis and hemorrhage in hematologic malignancy. Hematol Oncol Clin North Am. 1996;10:283–312.
74. Westwick J, Scully MF, Kakkar VV. Hemostatic imbalance in liver disease. Semin Thromb Hemost. 1992;18:155–165.

ISSN (O): 2687-5365; ISSN (P): 2753-6556