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Spectrum of Liver Diseases and Associated Coagulation Abnormalities: A Comprehensive Review

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ABSTRACT:

The liver is central to hemostasis, orchestrating the synthesis of coagulation factors, natural anticoagulants, fibrinolytic regulators, and thrombopoietin, while also clearing activated clotting proteins. Liver diseases disrupt these pathways, causing dynamic and often paradoxical hemostatic alterations. Traditionally considered hemorrhagic disorders due to prolonged prothrombin time (PT), international normalized ratio (INR), and thrombocytopenia, liver diseases are now recognized to induce a fragile equilibrium known as rebalanced hemostasis, which explains the simultaneous risk of bleeding and thrombosis. This comprehensive review examines coagulation abnormalities across the spectrum of liver disorders, including acute liver failure (ALF), chronic hepatitis, cirrhosis, metabolic dysfunction–associated steatotic liver disease (MASLD), cholestatic liver diseases, and vascular liver disorders. It discusses underlying pathophysiology, laboratory assessment using conventional and global hemostatic assays, clinical implications, and evidence-based management strategies. The review emphasizes individualized risk assessment, judicious transfusion, selective anticoagulation, and the integration of viscoelastic and thrombin generation testing into clinical practice. Finally, future research directions focusing on novel biomarkers, therapeutic targets, and outcome-based studies are highlighted.

1. INTRODUCTION

Hemostasis is a tightly regulated physiological process designed to maintain blood fluidity under normal conditions while enabling rapid clot formation after vascular injury. It involves platelets, coagulation factors, natural anticoagulants, fibrinolytic proteins, and the vascular endothelium. The liver plays a pivotal role in this process, synthesising the majority of plasma coagulation factors (fibrinogen, prothrombin, factors V, VII, IX–XIII), natural anticoagulants (protein C, protein S, antithrombin), and fibrinolytic regulators. Additionally, it produces thrombopoietin, the primary regulator of platelet production, and clears activated coagulation proteins and fibrin degradation products [1–3]. Hepatic sinusoidal endothelial cells and Kupffer cells further contribute to the regulation of hemostasis by internalizing tissue plasminogen activator (tPA), plasminogen activator inhibitor-1 (PAI-1), and activated coagulation complexes [4,5].

Historically, liver disease has been viewed predominantly as a hemorrhagic disorder due to prolonged PT, elevated INR, thrombocytopenia, and decreased fibrinogen. This perspective led to routine prophylactic transfusions of fresh frozen plasma (FFP) and platelets before invasive procedures. However, emerging clinical evidence has challenged this paradigm. Many patients with abnormal laboratory values undergo invasive procedures without significant bleeding, while paradoxical thrombotic events, including portal vein thrombosis (PVT), deep vein

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thrombosis (DVT), and pulmonary embolism (PE), occur despite prolonged PT/INR [6–8].

The concept of *rebalanced hemostasis* provides a mechanistic explanation for these paradoxes. In liver disease, simultaneous reductions in both procoagulant and anticoagulant factors create a fragile equilibrium, which can be tipped toward bleeding or thrombosis depending on disease severity, infections, renal dysfunction, or surgical stress [9–11]. Compensatory mechanisms, including elevated factor VIII and von Willebrand factor (vWF) levels, platelet activation, endothelial changes, and hypofibrinolysis, maintain effective hemostasis despite derangements in conventional coagulation tests [12–14].

Understanding these mechanisms is clinically essential. Misinterpretation of conventional coagulation assays may lead to unnecessary transfusions, increased thrombotic risk, and suboptimal procedural planning. The advent of global hemostatic assays, such as thrombin generation tests and viscoelastic methods (ROTEM and TEG), has improved the evaluation of coagulation status in liver disease, allowing for individualized, physiology-based patient management [15–17].

This review aims to provide a comprehensive synthesis of current knowledge on coagulation abnormalities across the spectrum of liver diseases, including acute liver failure, chronic hepatitis, cirrhosis, MASLD, cholestatic disorders, and vascular liver diseases. It explores pathophysiological mechanisms, laboratory evaluation, clinical manifestations, and modern management strategies, including transfusion guidance, anticoagulation, and emerging therapies. By consolidating recent evidence, this review seeks to enhance clinician understanding of the dynamic hemostatic changes in liver disease, facilitating safer and more effective patient care.

2. Physiology of Hepatic Hemostasis

2.1 Coagulation Factor Synthesis

The liver synthesizes fibrinogen (factor I), prothrombin (factor II), factors V, VII, IX, X, XI, XII, and XIII. Vitamin K–dependent factors (II, VII, IX, X) are particularly sensitive to hepatic dysfunction. Factor VII, with a half-life of 4–6 hours, declines early in liver disease, producing prolonged PT/INR, whereas fibrinogen remains preserved until advanced stages but may be structurally abnormal (dysfibrinogenemia) [18,19].

2.2 Natural Anticoagulants

Protein C, protein S, and antithrombin are synthesized by hepatocytes. Their reduction in liver disease partially counterbalances the loss of procoagulant factors, contributing to rebalanced hemostasis [20,21].

2.3 Platelet Production and Function

Thrombopoietin, primarily produced by hepatocytes, regulates platelet production. Liver dysfunction reduces thrombopoietin synthesis, contributing to thrombocytopenia. Platelets in liver disease may exhibit functional defects, including impaired aggregation, altered surface receptor expression, granule content abnormalities, and metabolic reprogramming. Elevated vWF partially compensates for reduced platelet number and function [22–24].

2.4 Fibrinolysis

Fibrinolysis is mediated by tPA, uPA, PAI-1, TAFI, and α2-antiplasmin. Cirrhosis is typically associated with hypofibrinolysis due to elevated PAI-1 and TAFI, whereas acute liver failure may demonstrate hyperfibrinolysis, contributing to increased bleeding risk [25–27].

2.5 Endothelial and Inflammatory Modulation

Endothelial activation in liver disease results in elevated vWF release and tissue factor expression, reduced nitric oxide availability, and systemic inflammatory cytokines (TNF-α, IL-6, IL-1β), all of which modulate hemostasis and increase thrombotic potential [28,29].

3. Pathophysiology of Coagulation Abnormalities

- **Reduced synthesis of coagulation factors:** Vitamin K–dependent (II, VII, IX, X) and non–vitamin–dependent (V, XI, XIII) factors decline progressively.
- **Anticoagulant deficiency:** Protein C, protein S, and antithrombin decrease.
- **Platelet abnormalities:** Thrombocytopenia, impaired aggregation, and storage pool deficiencies.

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- **Dysregulated fibrinolysis:**Hypofibrinolysis in cirrhosis vs. hyperfibrinolysis in acute liver failure.
- **Endothelial dysfunction:** Elevated vWF, tissue factor expression, and reduced nitric oxide availability.

4. Coagulation Abnormalities in Specific Liver Diseases

4.1 Acute Liver Failure

ALF is characterised by rapid hepatocellular necrosis with severe coagulopathy and encephalopathy. Factor VII declines first, followed by II, V, IX, X, and fibrinogen. Disseminated intravascular coagulation (DIC) and hyperfibrinolysis contribute to bleeding, including intracranial haemorrhage. Management includes etiologic therapy (e.g., N-acetylcysteine for acetaminophen toxicity), plasma exchange, extracorporeal support, and liver transplantation [30–33].

4.2 Cirrhosis

- **Compensated cirrhosis:**Hemostasis often preserved; low procedural bleeding risk.
- **Decompensated cirrhosis:** Ascites, variceal bleeding, renal dysfunction, and infections increase bleeding and thrombotic risk. Portal vein thrombosis, DVT, and PE are common [34–37].

4.3 Chronic Hepatitis

Early-stage chronic hepatitis usually preserves hemostasis. Advanced fibrosis causes PT/INR prolongation and thrombocytopenia. Autoimmune hepatitis may involve immune-mediated platelet destruction [38].

4.4 MASLD

MASLD is associated with systemic inflammation, platelet activation, endothelial dysfunction, and hypofibrinolysis. Macrophage-derived Factor XIII-A contributes to hepatic inflammation and fibrosis [39–41].

4.5 Cholestatic Liver Diseases

Vitamin K malabsorption in primary biliary cholangitis (PBC) or primary sclerosing cholangitis (PSC) causes reversible PT/INR prolongation. Advanced disease mirrors cirrhosis-associated hemostatic changes [42].

4.6 Vascular Liver Diseases

Budd–Chiari syndrome, sinusoidal obstruction syndrome, and portal vein thrombosis often require anticoagulation despite abnormal laboratory values [43–45].

5. Laboratory Assessment

- **Conventional coagulation tests:** PT, INR, and aPTT only reflect procoagulant factor deficiencies.
- **Thrombin generation assays:** Assess net coagulation potential and detect rebalanced hemostasis.
- **Viscoelastic assays (ROTEM/TEG):** Evaluate clot formation, strength, and lysis in whole blood; guide transfusion decisions [46–48].

6. Clinical Implications and Management

- Routine correction of PT/INR or platelet count is not recommended in the absence of bleeding.
- Individualised assessment of bleeding and thrombotic risk is essential.
- Anticoagulation is safe and indicated in selected cirrhotic patients with thrombotic events.
- Viscoelastic testing supports physiology-guided transfusion strategies.

7. Emerging Therapies and Future Directions

- Targeting Factor XIII-A and platelet activation in MASLD.
- Development of safer anticoagulants in cirrhosis for VTE prevention.
- Standardisation of viscoelastic-guided transfusion protocols.

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- Integration of global coagulation biomarkers into clinical practice.

8. CONCLUSION

Coagulation abnormalities in liver disease are dynamic and multifactorial. Rebalanced hemostasis explains the coexistence of bleeding and thrombotic events despite abnormal laboratory tests. Management should be individualised, guided by global hemostatic assays, and focus on judicious transfusion, selective anticoagulation, and risk stratification. Future research should prioritise prospective trials and novel therapeutic approaches.

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REFERENCES

1. Tripodi A, Mannucci PM. The coagulopathy of chronic liver disease. N Engl J Med. 2011;365:147–156.
2. Lisman T, Porte RJ. Rebalanced hemostasis in patients with liver disease: evidence and clinical consequences. Blood. 2010;116:878–885.
3. Caldwell SH, Hoffman M, Lisman T, et al. Coagulation Disorders and Hemostasis in Liver Disease: Pathophysiology and Management. Hepatology. 2006;44:1039–1046.
4. Northup PG, Caldwell SH. Coagulation in liver disease: a guide for the clinician. Clin Gastroenterol Hepatol. 2013;11:1064–1074.
5. Tripodi A, Salerno F, Chantarangkul V, et al. Evidence of normal thrombin generation in cirrhosis despite abnormal conventional coagulation tests. Hepatology. 2005;41:553–558.
6. De Pietri L, Bianchini M, Montalti R, et al. Thromboelastographic reference ranges for a cirrhotic population undergoing liver transplantation. World J Transplant. 2016;6:583–593.
7. Senzolo M, Burra P, Cholongitas E, et al. New insights into the coagulopathy of liver disease. World J Gastroenterol. 2006;12:7725–7736.
8. Lisman T, Bakhtiari K, Adelmeijer J, et al. Reduced plasma fibrinolytic potential in patients with cirrhosis due to altered balance of fibrinolytic proteins. J ThrombHaemost. 2013;11:474–480.
9. Tripodi A, Mannucci PM. Abnormalities of hemostasis in chronic liver disease: reappraisal of their clinical significance. J Hepatol. 2007;46:727–733.
10. Tripodi A. Hemostasis abnormalities in cirrhosis. Curr OpinHematol. 2015;22:406–412.
11. Bernal W, Wendon J. Acute liver failure. N Engl J Med. 2013;369:2525–2534.
12. Lee WM. Acute liver failure in the United States. Semin Liver Dis. 2003;23:217–226.
13. Stravitz RT, Lisman T. Coagulopathy, bleeding, and thrombosis in acute liver failure. Clin Liver Dis. 2018;22:271–285.
14. Stravitz RT, Kramer AH. Management of acute liver failure. Nat Rev Gastroenterol Hepatol. 2009;6:542–553.
15. Munoz SJ. Difficult management problems in fulminant hepatic failure. Semin Liver Dis. 1993;13:395–413.
16. Tripodi A, Primignani M, Lemma L, et al. Evidence that low protein C contributes to procoagulant imbalance in cirrhosis. J Hepatol. 2013;59:265–270.
17. Lisman T, Adelmeijer J, de Groot PG, et al. No evidence for an intrinsic platelet defect in patients with liver cirrhosis. Hepatology. 2006;44:84–90.
18. Kujovich JL. Hemostatic defects in end-stage liver disease. Crit Care Clin. 2005;21:563–587.
19. Peck-Radosavljevic M. Thrombocytopenia in liver disease. Liver Int. 2000;20(Suppl 3):60–66.

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www.jchr.org

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20. Giannini EG, Botta F, Borro P, et al. Platelet count/spleen diameter ratio: a non-invasive parameter to predict esophageal varices. Gut. 2003;52:1200–1205.

21. D'Amico G, Garcia-Tsao G, Pagliaro L. Natural history and prognostic indicators of survival in cirrhosis: a systematic review. J Hepatol. 2006;44:217–231.

22. Garcia-Tsao G, Bosch J. Management of varices and variceal hemorrhage in cirrhosis. N Engl J Med. 2010;362:823–832.

23. Abraldes JG, Villanueva C, Banares R, et al. Spanish consensus on portal hypertension. Gastroenterol Hepatol. 2012;35:421–450.

24. Northup PG, McMahon MM, Ruhl AP, et al. Coagulopathy does not fully protect hospitalized cirrhosis patients from venous thromboembolism. Am J Gastroenterol. 2006;101:1524–1528.

25. Søgaard KK, Horváth-Puhó E, Grønbaek H, et al. Risk of venous thromboembolism in patients with liver disease. Am J Gastroenterol. 2009;104:96–101.

26. Zhang X, Qi X, De Stefano V, et al. Epidemiology, risk factors, and in-hospital mortality of portal vein thrombosis in liver cirrhosis. Thromb Res. 2018;172:33–38.

27. Targher G, Byrne CD, Lonardo A, et al. Non-alcoholic fatty liver disease and risk of cardiovascular disease. Nat Rev Cardiol. 2016;13:81–96.

28. Verrijken A, Francque S, Mertens I, et al. Prothrombotic factors in non-alcoholic fatty liver disease. Hepatology. 2014;59:121–129.

29. Tripodi A, Branchi F, Chantarangkul V, et al. Hypercoagulability in patients with non-alcoholic fatty liver disease. J Hepatol. 2014;61:148–154.

30. Grover SP, Mackman N. Tissue factor: an essential mediator of hemostasis and trigger of thrombosis. ArteriosclerThrombVasc Biol. 2018;38:709–725.

31. Sherlock S, Dooley J. Diseases of the Liver and Biliary System. 12th ed. Oxford: Blackwell Science; 2011.

32. Andrade RJ, Lucena MI, Kaplowitz N, et al. Drug-induced liver injury: an update. Nat Rev Dis Primers. 2019;5:58.

33. Valla DC. Budd-Chiari syndrome and hepatic venous outflow tract obstruction. Semin Liver Dis. 2002;22:5–14.

34. DeLeve LD, Shulman HM, McDonald GB. Toxic injury to hepatic sinusoids: sinusoidal obstruction syndrome. Hepatology. 2002;36:706–716.

35. European Association for the Study of the Liver. EASL clinical practice guidelines: vascular diseases of the liver. J Hepatol. 2016;64:179–202.

36. Görlinger K, Dirkmann D, Hanke AA. Rotational thromboelastometry (ROTEM®). Scand J Clin Lab Invest. 2011;71(Suppl 243):3–15.

37. Whiting D, DiNardo JA. TEG and ROTEM: technology and clinical applications. Am J Hematol. 2014;89:228–232.

38. De Pietri L, Montalti R, Begliomini B. Thromboelastography-guided blood product use in cirrhosis. Hepatology. 2016;63:566–573.

39. Shah NL, Northup PG, Caldwell SH, et al. Portal vein thrombosis: current clinical practice. Clin Gastroenterol Hepatol. 2016;14:698–707.

40. Lisman T, Kamphuisen PW, Northup PG, et al. Established and new-generation antithrombotic drugs in patients with cirrhosis. J Hepatol. 2013;59:358–366.

41. Bernal W, Wendon J. Intensive care management of acute liver failure. Liver Int. 2013;33:155–167.

42. Hemker HC, Giesen P, Al Dieri R, et al. Calibrated automated thrombin generation measurement in plasma. PathophysiolHaemostThromb. 2003;33:4–15.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2026) 16(1), 145-150 | ISSN:2251-6727

43. Dargaud Y, Trzeciak MC, Bordet JC, et al. Use of thrombin generation assay in liver disease. Thromb Res. 2010;126:e33–e38.

44. Saner FH, Gieseler RK, Akiz H, et al. ROTEM in cirrhosis. Liver Int. 2013;33:929–935.

45. Tripodi A, Primignani M. Hypercoagulability in cirrhosis: evidence and clinical significance. J Hepatol. 2010;53:755–757.

46. Lisman T, Leebeek FWG. Hemostatic alterations in liver disease: clinical consequences and management. Dig Surg. 2007;24:250–258.

47. Stravitz RT, Lisman T. Hemostasis in acute liver failure. Clin Liver Dis. 2018;22:271–285.

48. Tripodi A, Mannucci PM. Coagulation in liver disease: reappraisal and clinical implications. J Hepatol. 2011;54:1415–1426.