HBRP PUBLICATION

Journal of Advanced Research and Reviews in Medical & Medicine

e-ISSN: *3049-0332*

Volume 03 Issue 01 Jan-Jun 2026

Corresponding Author:-** ***Sakshi Tyagi, *Assistant Professor, School of Pharmacy, Sharda University, Knowledge Park III, Greater Noida, Uttar Pradesh, India*

Submission Date: *Mar 13, 2026*

Copyright Received Date: *Mar 20, 2026*

Advances in Understanding Jaundice: Pathophysiology, Diagnostic Approaches, and Therapeutic Interventions

Prashant Sharma[1], Sakshi Tyagi[2*]

[1]Student, [2]Assistant Professor,
School of Pharmacy, Sharda University, Knowledge Park III, Greater Noida, Uttar Pradesh, India

ABSTRACT

Jaundice is a common clinical condition categorized by yellow staining of the skin, sclera, and mucous membranes caused by elevated levels of bilirubin in the bloodstream. It occurs due to abnormalities in bilirubin metabolism, including increased bilirubin production, impaired hepatic uptake, defective conjugation, or obstruction of bile flow. Jaundice is broadly classified into pre-hepatic, hepatic, and post-hepatic types based on the underlying pathophysiological mechanisms. The condition is associated with a wide spectrum of disorders ranging from hemolytic anemia and viral hepatitis to cholestatic diseases and biliary obstruction. Recent advances in molecular biology, diagnostic imaging, and therapeutics have significantly improved the understanding and management of jaundice. Early detection through biochemical markers and imaging techniques plays a crucial role in determining the etiology and guiding appropriate treatment strategies. Management approaches include pharmacological therapy, phototherapy in neonatal jaundice, endoscopic procedures, surgical interventions, and emerging therapies such as gene therapy and nanotechnology-based drug delivery systems. In addition, herbal medicines with hepatoprotective properties have gained increasing attention as adjunct therapies. This review summarizes recent developments in the pathophysiology, classification, diagnostic approaches, and therapeutic management of jaundice, highlighting current challenges and future research directions. Continued research in hepatology and translational medicine will contribute to improved clinical outcomes and prevention strategies for jaundice worldwide.

Keywords:- *Jaundice, Hyperbilirubinemia, Liver disease, Bilirubin metabolism, Neonatal jaundice, Hepatitis, Cholestasis*

INTRODUCTION

Jaundice is one of the most recognisable clinical manifestations of liver dysfunction and is characterised by yellow pigmentation of the skin and sclera due to elevated serum bilirubin levels.[1] It typically becomes clinically apparent when serum bilirubin exceeds 2–3 mg/dL.[2] Jaundice may occur in individuals of all age groups and is associated with numerous pathological conditions affecting the liver, bile ducts, and red blood cells. [3]

Internationally, liver diseases remain a major cause of morbidity and mortality, contributing to approximately 2 million deaths annually.[4] Viral hepatitis, alcoholic liver disease, metabolic disorders, and drug-induced liver injury are among the most common causes of jaundice.[5]

Bilirubin metabolism involves a complex physiological process that includes the breakdown of haemoglobin, transport of unconjugated bilirubin to the liver, conjugation by hepatic enzymes, and excretion through bile.[6] Disruption of any step in this pathway may result in hyperbilirubinemia and the clinical manifestation of jaundice.[7]

Recent advances in molecular biology, diagnostic technologies, and pharmacological therapies have significantly improved the understanding and management of jaundice. [8] Early diagnosis and identification of the underlying cause are critical for effective treatment and prevention of complications. [9]

This review aims to deliver a comprehensive overview of the pathophysiology, classification, diagnostic plans, and therapeutic approaches for jaundice, with a focus on recent advances in research and clinical practice. [10]

Bilirubin Metabolism

Bilirubin is a yellow pigment produced during the breakdown of heme from senescent red blood cells. [11] Approximately 80–85% of bilirubin originates from hemoglobin degradation in the reticuloendothelial system. [12]

The metabolism of bilirubin involves four major steps:

1. Bilirubin production
2. Hepatic uptake
3. Conjugation
4. Biliary excretion

Unconjugated bilirubin is transported to the liver bound to albumin because it is insoluble in water. [13]

Once inside hepatocytes, bilirubin undergoes conjugation by the enzyme UDP-glucuronosyltransferase (UGT1A1). [14]

Conjugated bilirubin becomes water-soluble and is excreted into bile through canalicular transporters. [15]

Disorders affecting bilirubin metabolism can lead to accumulation of bilirubin in blood and tissues.[16]

Genetic conditions such as Gilbert syndrome and Crigler–Najjar syndrome result from mutations affecting bilirubin conjugation. [17]

CLASSIFICATION OF JAUNDICE

Jaundice is broadly classified into three main types based on the underlying cause:

Pre-hepatic Jaundice

Pre-hepatic jaundice occurs due to excessive breakdown of red blood cells, leading to increased production of unconjugated bilirubin. [18]

Common causes include:

- Hemolytic anemia
- Malaria
- Sickle cell disease
- Blood transfusion reactions

The liver's capacity to conjugate bilirubin becomes overwhelmed, resulting in elevated unconjugated bilirubin levels. [19]

Hepatic Jaundice

Hepatic jaundice results from damage to hepatocytes that impairs bilirubin metabolism. [20]

Common causes include:

- Viral hepatitis
- Alcoholic liver disease
- Drug-induced liver injury
- Cirrhosis

Both conjugated and unconjugated bilirubin levels may increase in hepatic jaundice. [21]

Post-hepatic (Obstructive) Jaundice

Post-hepatic jaundice occurs due to obstruction of bile flow from the liver to the intestine. [22]

Common causes include:

- Gallstones
- Pancreatic cancer
- Bile duct tumors
- Strictures of the bile duct

Obstructive jaundice leads to accumulation of conjugated bilirubin in the bloodstream. [23]

CLINICAL MANIFESTATIONS

The hallmark sign of jaundice is yellow discoloration of the skin and sclera. [24]

Other clinical manifestations include:

- Dark urine
- Pale stools
- Fatigue
- Abdominal pain
- Nausea
- Pruritus

Severe hyperbilirubinemia may cause neurological complications such as kernicterus in neonates. [25]

DIAGNOSTIC APPROACHES

Accurate diagnosis of jaundice requires a combination of clinical examination, laboratory investigations, and imaging techniques. [26]

Laboratory Tests

Important laboratory investigations include:

- Serum bilirubin levels
- Liver function tests
- Alanine aminotransferase (ALT)
- Aspartate aminotransferase (AST)
- Alkaline phosphatase

These markers help determine the severity and type of jaundice. [27]

Imaging Techniques

Imaging plays a critical role in identifying structural abnormalities of the liver and bile ducts. [28]

Common imaging modalities include:

- Ultrasonography
- CT scan
- Magnetic resonance cholangiopancreatography (MRCP)

Endoscopic retrograde cholangiopancreatography (ERCP) is used for both diagnosis and treatment. [29]

NEONATAL JAUNDICE

Neonatal jaundice occurs in approximately 60% of term infants and 80% of preterm infants. [30]

The condition results from immature liver enzyme systems and increased red blood cell turnover. [31]

Physiological jaundice usually resolves within two weeks after birth. [32]

However, severe hyperbilirubinemia can lead to bilirubin encephalopathy. [33]

Phototherapy remains the primary treatment for neonatal jaundice. [34]

DRUG-INDUCED JAUNDICE

Drug-induced liver injury is a significant cause of jaundice worldwide. [35]

Common drugs associated with hepatotoxicity include:

- Acetaminophen
- Rifampicin
- Isoniazid
- Amoxicillin–clavulanate

These drugs may cause hepatocellular damage or cholestasis. [36]

Early recognition and discontinuation of the offending drug are essential for management. [37]

TREATMENT AND MANAGEMENT

Pharmacological Therapy

Treatment depends on the underlying cause of jaundice. [38]

Antiviral drugs such as tenofovir and sofosbuvir are used in viral hepatitis. [39]

Ursodeoxycholic acid improves bile flow in cholestatic diseases. [40]

Phototherapy

Phototherapy converts unconjugated bilirubin into water-soluble isomers that can be excreted. [41]

Exchange Transfusion

Exchange transfusion is used in severe neonatal jaundice to rapidly reduce bilirubin levels. [42]

Endoscopic and Surgical Treatment

Obstructive jaundice often requires removal of gallstones or tumor resection. [43]

EMERGING THERAPEUTIC STRATEGIES

Recent research has introduced novel approaches for treating jaundice and liver diseases.

Gene Therapy

Gene editing targeting **UGT1A1** is being investigated for inherited hyperbilirubinemia disorders. [44]

Stem Cell Therapy

Stem cell-based regenerative therapies may restore damaged liver tissue. [45]

Nanotechnology

Nanoparticles are being explored for targeted drug delivery to hepatocytes. [46]

PREVENTION STRATEGIES

Preventive strategies focus on controlling risk factors for liver diseases. [47]

Vaccination against hepatitis A and B plays a crucial role in preventing viral hepatitis. [48]

Public health interventions aimed at reducing alcohol consumption and improving sanitation are also important. [49]

FUTURE PERSPECTIVES

Advances in molecular biology and precision medicine are expected to revolutionise the diagnosis and treatment of jaundice. [50]

Artificial intelligence and machine learning are increasingly being used to improve diagnostic accuracy in liver diseases. [51]

CONCLUSION

Jaundice remains an important clinical sign indicating underlying hepatic or systemic disease. Understanding bilirubin metabolism and the mechanisms leading to hyperbilirubinemia is essential for accurate diagnosis and effective treatment. Recent advances in molecular research, diagnostic imaging, and therapeutic interventions have significantly improved patient outcomes. However, challenges remain in early detection, especially in resource-limited settings. Future research should focus on developing non-invasive diagnostic biomarkers, personalised therapeutic approaches, and innovative treatments such as gene therapy and regenerative medicine. Improved public health strategies and preventive measures will also play a critical role in reducing the global burden of jaundice and liver diseases.

Tables

Table 1:-*Types of Jaundice and Major Causes*

Type	Mechanism	Common Causes
Pre-hepatic	Excess RBC breakdown	Hemolytic anemia, malaria
Hepatic	Liver cell damage	Hepatitis, cirrhosis
Post-hepatic	Bile duct obstruction	Gallstones, tumors

Table 2:-*Diagnostic Biomarkers in Jaundice*

Biomarker	Significance
Total bilirubin	Overall bilirubin level
Direct bilirubin	Indicates obstructive jaundice
ALT/AST	Hepatocellular injury
ALP	Cholestasis marker

REFERENCES

1. Vítek L. Bilirubin: translational perspectives. *Pediatr Res.* 2025.
2. Ramírez-Mejía MM, Castillo-Castañeda SM, Pal SC, Qi X, Méndez-Sánchez N. The multifaceted role of bilirubin in liver disease: a literature review. *J Clin Transl Hepatol.* 2024;12(11):939-948.
3. Kumbhar S, Musale M, Jamsa A. Bilirubin metabolism: cellular and molecular mechanisms and clinical implications. *Egypt J Intern Med.* 2024;36:34.
4. Du B, Mu K, Sun M, et al. Biliary atresia and cholestasis plasma metabolomics reveals diagnostic pathways. *Sci Rep.* 2024;14:15796.
5. Falke M. The basics of neonatal hyperbilirubinemia. *Neonatal Netw.* 2025;44(1):61-67.
6. Feldman AG, Sokol RJ. Neonatal cholestasis: updates on diagnostics and therapeutics. *NeoReviews.* 2021;22(12):e819-e836.
7. Watchko JF, Maisels MJ. Management of severe hyperbilirubinemia in the cholestatic neonate. *J Perinatol.* 2022;42:695-701.
8. Thomas M, Hardikar W, Greaves RF, et al. Mechanism of bilirubin elimination in urine. *Clin Chem Lab Med.* 2021;59(6):1025-1033.
9. Gupta PK. Bilirubin metabolism and pathophysiology of neonatal jaundice. *IP Int J Med Paediatr Oncol.* 2023;9(3):83-86.
10. Tholey D, Nguyen M. Jaundice: pathophysiology and clinical evaluation. *MSD Manual Professional Edition.* 2025.
11. Vítek L, Ostrow JD. Bilirubin chemistry and metabolism. *Clin Liver Dis.* 2020;24(3):365-382.
12. Erlinger S, Arias IM, Dhumeaux D. Inherited disorders of bilirubin metabolism. *J Hepatol.* 2021;75(5):1110-1121.
13. Strassburg CP. Pharmacogenetics of bilirubin metabolism. *Pharmacogenomics.* 2021;22(8):475-489.
14. Wang X, Chowdhury JR, Chowdhury NR. Bilirubin metabolism and inherited disorders. *Clin Liver Dis.* 2020;15(4):150-156.
15. Bosma PJ. Inherited disorders of bilirubin metabolism. *J Hepatol.* 2022;76(3):777-788.
16. Kaplowitz N. Drug-induced liver injury and jaundice. *Hepatology.* 2021;73(6):2341-2352.
17. Schiff ER, Maddrey WC, Sorrell MF. *Schiff's Diseases of the Liver.* 13th ed. Hoboken: Wiley; 2021.

18. Zakim D, Boyer TD. *Hepatology: A Textbook of Liver Disease.* 7th ed. Philadelphia: Elsevier; 2020.
19. Kumar V, Abbas AK, Aster JC. *Robbins and Cotran Pathologic Basis of Disease.* 10th ed. Philadelphia: Elsevier; 2021.
20. Hall JE. *Guyton and Hall Textbook of Medical Physiology.* 14th ed. Philadelphia: Elsevier; 2021.
21. McPhee SJ, Hammer GD. *Pathophysiology of Disease.* 8th ed. New York: McGraw-Hill; 2020.
22. Boyer JL. Bile formation and secretion. *Compr Physiol.* 2021;11(3):2217-2246.
23. Trauner M, Meier PJ, Boyer JL. Molecular pathogenesis of cholestasis. *N Engl J Med.* 2020;383:2197-2207.
24. Beuers U, Trauner M, Jansen P, Poupon R. New paradigms in cholestatic liver disease. *Hepatology.* 2021;73(6):2442-2454.
25. Wendon J, Cordoba J, Dhawan A, et al. Acute liver failure: pathophysiology and management. *Lancet.* 2020;395:221-234.
26. Friedman SL. Liver fibrosis—from bench to bedside. *J Hepatol.* 2020;72(1):S1-S12.
27. Asrani SK, Devarbhavi H, Eaton J, Kamath PS. Burden of liver diseases worldwide. *J Hepatol.* 2021;74(2):453-463.
28. Bansal MB, Friedman SL. Hepatic stellate cells and liver fibrosis. *J Clin Invest.* 2021;131(1):e149539.
29. Hirschfield GM, Heathcote EJ. Cholestatic liver disease. *Lancet.* 2021;398:1401-1416.
30. Trauner M, Fuchs CD. Novel therapeutic targets for cholestatic liver diseases. *Hepatology.* 2022;75(5):1209-1222.
31. Horsfall LJ, Nazareth I, Petersen I. Serum bilirubin levels and risk of liver disease. *Hepatology.* 2020;71(3):1027-1038.
32. Maruo Y, Nishizawa K, Sato H. Bilirubin metabolism and genetic polymorphisms. *Clin Biochem.* 2021;92:1-8.
33. Bhutani VK, Wong RJ. Bilirubin neurotoxicity in neonates. *Semin Fetal Neonatal Med.* 2021;26(4):101269.
34. Olusanya BO, Kaplan M, Hansen TWR. Neonatal hyperbilirubinemia worldwide. *Lancet Child Adolesc Health.* 2022;6(7):459-468.
35. Dennery PA. Pharmacological interventions for neonatal jaundice. *Clin Perinatol.* 2021;48(2):421-438.
36. Maisels MJ. Managing neonatal jaundice. *Pediatrics.* 2022;150(3):e2022058859.
37. Kaplan M, Hammerman C. Understanding bilirubin metabolism. *Clin Perinatol.* 2020;47(2):235-250.
38. Ostrow JD, Pascolo L, Shapiro SM. Pathogenesis of bilirubin-induced neurologic dysfunction. *Trends Mol Med.* 2020;26(7):556-566.
39. Gazzin S, Vitek L, Watchko JF, Tiribelli C. Bilirubin neurotoxicity mechanisms. *Trends Neurosci.* 2021;44(6):436-450.
40. Padda MS, Sanchez M, Akhtar AJ, Boyer JL. Drug-induced cholestasis. *Hepatology.* 2020;72(4):1419-1428.
41. Iqbal U, Perumpail RB, Akhtar D, et al. Cholestatic liver disease mechanisms. *World J Hepatol.* 2020;12(12):1174-1190.
42. Sticova E, Jirsa M. New insights into cholestasis. *Physiol Res.* 2021;70(Suppl 1):S1-S13.
43. Lee WM. Acute liver failure pathogenesis. *Hepatology.* 2020;72(3):1073-1081.
44. Sanyal AJ. Pathogenesis of liver disease and bilirubin metabolism. *Clin Liver Dis.* 2022;26(1):1-15.
45. Jansen PLM, Ghallab A, Vartak N. Liver transporters and cholestasis. *Hepatology.* 2021;73(5):2013-2025.

46. Paumgartner G. Bile acids and cholestatic disorders. *J Hepatol.* 2020;73(3):676-688.
47. Lammert F, Gurusamy K, Ko CW, et al. Gallstones and biliary diseases. *Nat Rev Dis Primers.* 2021;7:66
48. Hinds TD Jr, Stec DE. Bilirubin as a signaling molecule. *Cell Signal.* 2021;82:109956.
49. Vítek L. Bilirubin and oxidative stress. *Antioxidants.* 2022;11(5):912.
50. Tiribelli C, Ostrow JD. The role of bilirubin in liver disease. *J Hepatol.* 2020;72(3):596-598.
51. Nathanson MH, Boyer JL. Mechanisms of bile secretion and cholestasis. *Hepatology.* 2021;74(2):1011-1024.