WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

A COMPREHENSIVE REVIEW ON THE THERAPEUTIC ROLE IN JAUNDICE MANAGEMENT

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ABSTRACT:

Jaundice refers to the yellow discoloration of the skin, sclera, and mucous membranes caused by elevated bilirubin levels in the blood. It is a clinical sign rather than a disease and results from disturbances in bilirubin metabolism. Jaundice is classified into **pre-hepatic (hemolytic), hepatic (hepatocellular), and post-hepatic (obstructive)** types depending on the underlying mechanism. Etiologies include congenital and acquired disorders, such as hemolytic anemias, viral hepatitis, genetic enzyme deficiencies, gallstones, tumors, and neonatal liver immaturity. Elevated bilirubin may cause systemic complications, including bilirubin encephalopathy in neonates, renal injury, coagulopathy, immunosuppression, and cholangitis. Diagnosis requires biochemical tests, imaging, and sometimes invasive procedures. Treatment depends on etiology and involves phototherapy, exchange transfusion, medications, nutritional support, and surgical/endoscopic interventions. Early diagnosis and timely management are critical to prevent complications and improve outcomes.

Keywords: Jaundice, Hyperbilirubinemia, Hepatobiliary obstruction, Hemolysis, Neonatal jaundice, Bilirubin metabolism

1. INTRODUCTION

Jaundice arises from the accumulation of bilirubin—a yellow pigment produced from hemoglobin breakdown. Under normal physiology, bilirubin undergoes hepatic uptake, conjugation, and excretion. Serum bilirubin >2–3 mg/dL becomes clinically detectable as scleral icterus. Jaundice is common in neonates due to immature hepatic enzymes and may indicate serious hepatobiliary or hematological disease in adults.

Mechanistically, jaundice is categorized as:

1.1 Pre-hepatic (Hemolytic) Jaundice

Excessive red blood cell destruction overwhelms the liver's conjugation capacity, increasing **unconjugated bilirubin**.

1.2 Hepatic (Hepatocellular) Jaundice

Hepatocyte dysfunction impairs bilirubin uptake, conjugation, or excretion. Viral hepatitis, cirrhosis, alcohol, and genetic enzyme defects are common causes.

1.3 Post-hepatic (Obstructive) Jaundice

Extrahepatic biliary obstruction prevents bilirubin passage into the intestine, raising **conjugated bilirubin**.

Systemic manifestations include fatigue, pruritus, dark urine, pale stools, malabsorption, coagulopathy, and organ dysfunction. Diagnosis integrates liver function testing, bilirubin fractionation, ultrasonography, CT/MRI, MRCP, or ERCP. Management is cause-specific and ranges from conservative therapy to surgical decompression.

2. BILIRUBIN PRODUCTION AND METABOLISM

Bilirubin undergoes three principal phases:

2.1 Pre-hepatic Phase

- 80% derived from RBC breakdown; remainder from myoglobin/cytochrome metabolism.
- Unconjugated bilirubin binds albumin in plasma.

2.2 Intrahepatic Phase

- Hepatocytes conjugate bilirubin via **UDP-glucuronosyltransferase (UGT1A1)**.
- Conjugated bilirubin becomes water-soluble.

2.3 Post-hepatic Phase

- Conjugated bilirubin enters bile → intestine.
- Converted to urobilinogen, excreted via stool (as stercobilin) or urine (as urobilin).

Obstruction or metabolic defects in any phase lead to hyperbilirubinemia.

3. TYPES OF JAUNDICE

3.1 Pre-hepatic Jaundice (Hemolytic)

Congenital causes:

- Spherocytosis, elliptocytosis, thalassemia, G6PD deficiency, sickle cell disease, Crigler-Najjar, etc.

Acquired causes:

- Autoimmune hemolysis, infections (malaria), toxins, drug reactions, hematoma resorption, DIC, trauma.

Clinical features often include anemia, fatigue, splenomegaly, and elevated unconjugated bilirubin.

3.2 Hepatic Jaundice

Results from hepatocyte dysfunction or impaired bilirubin conjugation.

Congenital causes:

- Gilbert syndrome, Crigler-Najjar, Wilson's disease, Dubin-Johnson, Rotor syndrome.

Acquired causes:

- Viral hepatitis, alcoholic hepatitis, autoimmune hepatitis, drugs (NSAIDs), sepsis, pregnancy, malnutrition, tumors.

UGT1A1 deficiency (e.g., in neonates) contributes significantly to physiological jaundice.

3.3 Post-hepatic (Obstructive) Jaundice

Caused by obstruction of the biliary tract.

Congenital causes:

- Biliary atresia, choledochal cysts, cystic fibrosis.

Acquired causes:

- Gallstones, pancreatitis, tumors (pancreatic, cholangiocarcinoma), strictures, tuberculosis, AIDS cholangiopathy, trauma.

Leads to high conjugated bilirubin, pruritus, pale stools, dark urine.

4. NEONATAL JAUNDICE

Neonatal jaundice appears in **60% of term infants** and **80% of preterm infants**. It includes:

4.1 Physiological Jaundice

- Appears on day 2–4, resolves by day 10–14.
- Caused by immature UGT1A1 and increased RBC turnover.

4.2 Breast Milk Jaundice

- Due to β-glucuronidase in breast milk, increased enterohepatic circulation.

4.3 Pathological Jaundice

Causes include:

- Hemolysis (ABO/Rh incompatibility)
- Sepsis
- Crigler-Najjar, Gilbert syndrome
- Biliary atresia
- Endocrine disorders (hypothyroidism)

4.4 Bilirubin Encephalopathy (Kernicterus)

Occurs when unconjugated bilirubin crosses the blood–brain barrier.

Symptoms:

- Lethargy, poor feeding, high-pitched cry, opisthotonus, seizures.

MRI shows T2 hyperintensity in globus pallidus.

5. PATHOPHYSIOLOGY AND SYSTEMIC EFFECTS

Jaundice affects various organs:

5.1 Biliary System

- Increased ductal pressure → bile stasis, infection, cholangitis.

5.2 Liver

- Hepatocyte necrosis, fibrosis, ductal proliferation.

5.3 Kidneys

- Bile acid nephropathy → acute kidney injury.

5.4 Gut

- Loss of bile flow → bacterial overgrowth → endotoxemia.

5.5 Immune System

- Reduced Kupffer cell activity → susceptibility to sepsis.

5.6 Coagulation

- Vitamin K malabsorption → bleeding risk.
- Hypercoagulability due to NET formation.

6. CLINICAL FEATURES

6.1 Adults

- Yellow skin/eyes
- Dark urine, pale stools
- Itching
- Fatigue, anorexia, nausea
- Abdominal pain
- Fever (suggestive of cholangitis)

- Weight loss (malignancy indicator)

6.2 Newborns

- Yellow skin/eyes starting from face
- Poor feeding, lethargy
- Dark urine, pale stools
- Severe signs: fever, arching, seizures (risk of encephalopathy)

7. DIAGNOSIS

7.1 Laboratory Tests

- Total, direct, indirect bilirubin
- Liver function tests (ALT, AST, ALP, GGT)
- CBC, reticulocyte count, Coombs test

7.2 Imaging

- Ultrasound
- CT/MRI
- MRCP/ERCP

7.3 Advanced Tests

- Genetic testing (UGT1A1, BSEP, MDR3)
- Liver biopsy when necessary

8. TREATMENT

Treatment is cause-specific.

8.1 Pre-hepatic Jaundice

- Treat hemolysis
- Manage anemia, transfusions
- Avoid triggers in G6PD deficiency

8.2 Hepatic Jaundice

- Antivirals (for hepatitis)
- Steroids for autoimmune hepatitis
- Nutritional support
- Hepatoprotective therapy

8.3 Post-hepatic (Obstructive) Jaundice

Medical Management

- Pain management (avoid NSAIDs in cirrhosis)
- Antibiotics for cholangitis
- Antiemetics
- Pruritus control: Ursodeoxycholic acid, cholestyramine, rifampin, sertraline, opioid antagonists

Endoscopic & Interventional Treatments

- ERCP with stenting
- Endoscopic nasobiliary drainage
- EUS-guided biliary drainage
- Mechanical decompression for obstruction

Surgical Treatment

- Laparoscopic common bile duct exploration
- Pancreaticoduodenectomy (for malignancy)
- Roux-en-Y choledochojejunostomy (palliative)

9. MANAGEMENT OF NEONATAL JAUNDICE

9.1 Phototherapy

- Converts bilirubin to water-soluble isomers
- Blue-green (475–490 nm) light most effective
- Continuous vs intermittent depending on severity

9.2 Exchange Transfusion

- For severe hemolytic jaundice
- Removes bilirubin and antibodies

9.3 Pharmacologic Therapy

- Intravenous immunoglobulin (IVIG) for hemolysis
- Albumin infusion to bind free bilirubin

10. CONCLUSION

Jaundice is a multifactorial clinical sign with diagnostic and prognostic significance. Understanding bilirubin metabolism, etiological classification, and systemic implications is essential for accurate diagnosis and management. Early recognition—especially in neonates—prevents life-threatening complications such as kernicterus or multi-organ failure. Advances in imaging, molecular diagnostics, and minimally invasive interventions continue to improve outcomes in jaundice management.

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