Understanding Jaundice in Children: Causes, Symptoms and Management

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Abstract

Jaundice, characterized by yellowing of the skin, sclera, and mucous membranes, results from elevated bilirubin levels, primarily due to red blood cell breakdown and immature bilirubin metabolism in new-borns. It affects 60% of term and 80% of preterm neonates globally, often resolving naturally, though severe cases may lead to kernicterus and long-term disabilities. Causes include physiological immaturity, haemolytic disorders (e.g., G6PD deficiency, iso-immune haemolysis), liver dysfunction (e.g., NAFLD, sepsis, or drug-induced damage), biliary obstruction, and genetic conditions like Gilbert syndrome. Environmental factors, poor nutrition, and toxins also increase risk. Symptoms range from yellow skin and sclera to anaemia, dark urine, and pale faeces, depending on the underlying cause. Diagnosis involves clinical assessment and the measurement of bilirubin levels using biochemical methods, bilirubin meters, or transcutaneous bilirubin meters. Also includes differentiation between physiological and pathological jaundice. Management includes phototherapy, exchange transfusion, and pharmacological interventions like phenobarbitone and IVIG, tailored to the severity and aetiology. Early identification, parental education, and follow-up are crucial in preventing complications and ensuring better outcomes.

Keywords: Jaundice, Hyperbilirubinemia, New-born, children, phototherapy, Causes, Management

Cite this Article as: Binyamin A, Jabeen F, Riaz F, Ali SS, Amjad H, Ahmad M and Khan T, 2025. Understanding jaundice in children: causes, symptoms and management. In: Ismael SS, Nisa QU, Nisa ZU and Aziz S (eds), Diseases Across Life: From Humans to Land and Sea. Unique Scientific Publishers, Faisalabad, Pakistan, pp: 264-270. https://doi.org/10.47278/book.HH/2025.188

A Publication of Unique Scientific Publishers

Chapter No: 25-038

Received: 07-Feb-2025
Revised: 17-March-2025
Accepted: 20-Apr-2025

Introduction

Jaundice is a condition characterized by the yellowing of the skin, mucous membranes, and sclera due to the accumulation of bilirubin, a yellow-orange bile pigment. The term “jaundice” comes from the French word *jaune*, meaning “yellow” (Ansong-Assoku et al., 2025). It is a visible sign of hyperbilirubinemia, which can occur in either a conjugated or an unconjugated form. Jaundice becomes clinically noticeable when bilirubin levels exceed 34.2 µmol/L (2 mg/dL) (Mahgoub et al., 2023). Bilirubin (BR), a by-product of the breakdown of the haem tetrapyrrolic ring, primarily originates from the destruction of red blood cells (RBCs), accounting for about 80%, while the remaining 20% comes from inefficient erythropoiesis, muscle myoglobin breakdown, and liver cytochromes (Sticova & Jirsa, 2013).

BR is not just a harmful molecule with serious consequences; like uric acid, it plays a vital role as an antioxidant in the neonatal biological system (Soto Conti, 2021). However, excessively high BR levels can be toxic to central nervous system development, potentially leading to behavioural and neurological impairments, including neurotoxicity or kernicterus, even in full-term new-borns (Hokkanen et al., 2014). Different types of bilirubinaemia are reported in new-borns and children such as physiological, pathological, or jaundice due to breastfeeding or haemolysis.

Jaundice has been shown to afflict at least 60% of full-term and 80% of preterm neonates (Lake et al., 2019). Indicating that about 84–112 million of the approximately 140 million babies born each year worldwide (UNICEF, 2017) will diagnosed with jaundice within the first two weeks of birth. Clinical jaundice is less common in older children and adolescents than in new-borns (Muniyappa & Kelley, 2020). The TSB threshold for clinically severe jaundice varies depending on factors such as postnatal age, race, co-morbid preterm, sepsis, and haemolytic diseases (Lake et al., 2019). In older children, it can be conjugated or unconjugated hyperbilirubinemia due to different causes (Muniyappa & Kelley, 2020).

Although newborn jaundice is common, most affected infants recover without complications. Elevated unconjugated BR levels in certain neonates may lead to acute and chronic BR encephalopathy, known as kernicterus, which can cause irreversible brain damage (Aggarwal et al., 2017) and death (Olusanya et al., 2016). Jaundice can cause serious impairments in infants, including cerebral palsy, mental retardation, and deafness if it is not identified and treated early in life (Ezeaka et al., 2014). This chapter explores jaundice in children, covering its causes, symptoms, diagnosis, and management. It differentiates between physiological and pathological jaundice, highlights risk factors, and outlines key symptoms for early recognition. Readers will learn about diagnostic methods, treatment options like phototherapy, and urgent care needed. Prevention strategies and complications, such as kernicterus, are also discussed to give a full understanding of the topic.

Bilirubin Metabolism

BR is the final product of the heme breakdown process in animals. Heme oxygenase metabolizes heme into Biliverdin (BV), carbon monoxide, and ferrous iron (Duvigneau et al., 2019). Biliverdin reductase further reduces BV, a polar and harmless molecule, to unconjugated BR. Conversion of BV to BR may be recycled by oxidation of BR to BV, resulting in an amplified impact of BR (Valášková & Muchová, 2016). Since most vertebrates synthesize only BV, it is postulated that only BR can overcome the placental barrier via diffusion due to its relative hydrophobicity. This action is thought to prevent the accumulation of BV in foetuses (Robinson et al., 2021).

Most of the unconjugated BR is transported to the liver to prevent its harmful effects (Valášková & Muchová, 2016). Unjugated BR exists in equilibrium with the albumin-bound form. Only a small fraction (<0.01%) of BR remains unbound (Bf) in the plasma, and as it is water insoluble, it circulates in the bloodstream. This unbound BR is primarily responsible for its pathophysiological effects on cells and tissues (Amin, 2016). UCB enters liver cells through passive diffusion, facilitated by transporters OATP1B1 and 1B3 (Kumbhar et al., 2024). UDP-glucuronosyltransferase (UGT1A1) in hepatocytes makes UCB water-soluble, which is initially low at birth and increases over three months (Hansen et al., 2020). This process is influenced by hormones, with progesterone enhancing and testosterone reducing enzyme activity (Abbas et al., 2016). Hepatocytes of the endoplasmic reticulum conjugate BR and actively transport it into the bile (Valášková & Muchová, 2016) primarily by ABCC2, with ABCG2 potentially playing a supporting role (Roma et al., 2008). Some CB re-enters the bloodstream, forming a "sinusoidal liver-to-blood loop," a process that is less efficient in infants due to lower OATP1B1 and OATP1B3 expression compared to adults (Mooij et al., 2014).

In the intestines, gut bacteria convert most bilirubin into urobilinogen and stercobilinogen, which are then released in faeces as stercobilin and urobilin. Some urobilinogen undergoes enterohepatic circulation, appearing in urine (Fevery, 2008), and UCB may be reabsorbed from the colon and returned to the liver (Guerra Ruiz et al., 2021). Figure 1 shows a summary of BR metabolism.

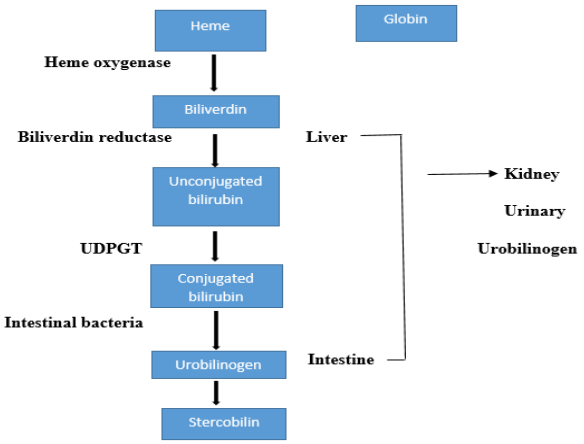

Fig. 1: After the breakdown of red blood cells, BR transports to the liver and combines with the albumin. Hepatocytes absorb BR, which is then conjugated and sent to the stomach by bile (Mahgoub et al., 2023).

Causes and Pathophysiology

Pathophysiology

Jaundice described as yellowish staining of the sclera caused by improper BR metabolism. Obstructive jaundice occurs when the normal flow of bile from the liver to the gallbladder and then to the small intestine is disrupted. Elevated total BR levels rise in either the conjugated or the unconjugated form, depending on the degree of BR metabolism disruption.

This disturbance might occur on three different levels. In pre-hepatic jaundice, excessive BR synthesis exceeds the liver's ability to conjugate and eliminate it into the intestines, resulting in a majority of unconjugated BR. The most prevalent cause of pre-hepatic jaundice is haemolytic anaemia, a disorder characterized by an excessive breakdown of heme.

Intrahepatic jaundice mostly occurs due to liver parenchymal disease, which reduces the liver's capacity to conjugate or eliminate BR. This causes the conjugated BR fraction to rise first, followed by the unconjugated component. Common causes include viral hepatitis, drug-induced liver damage, and primary biliary cirrhosis.

Post-hepatic jaundice, also known as obstructive jaundice, arises when bile flow is restricted due to a partial or complete obstruction of the extrahepatic biliary channels between the liver and the duodenum. This causes a prevalence of conjugated hyperbilirubinemia, a hallmark feature of obstructive jaundice.

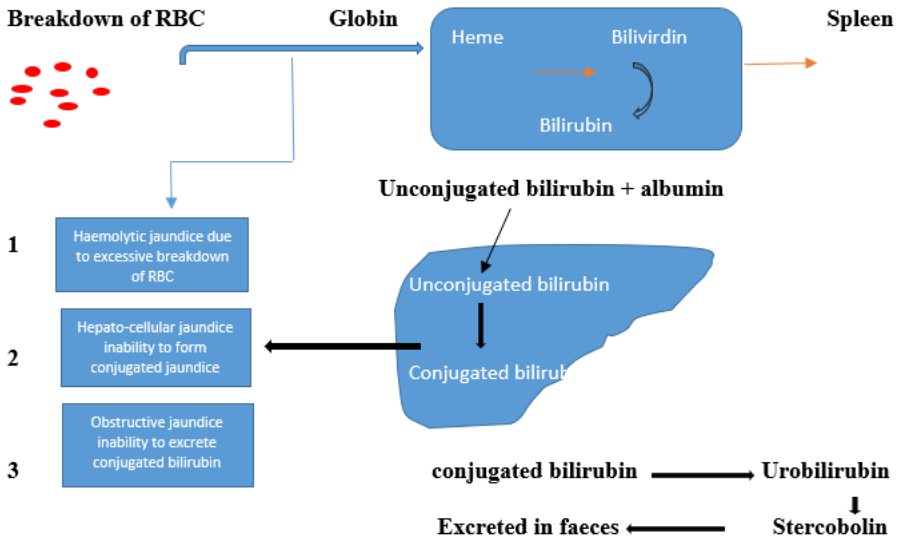

Fig. 2: Pathophysiology of jaundice (Janghel et al., 2019).

Physiological Causes

This condition occurs due to new-borns' physiological immaturity in handling high BR levels, which leads to visible jaundice between 24-72 hours of age. TSB levels below 2 mg/dL may not be seen until one month in both full-term and preterm babies. Safe levels of BR differ based on the gestational period (Itoh et al., 2023).

Haemolytic Causes

The 2004 American Academy of Paediatrics (AAP) recommendations for treating hyperbilirubinemia ("Management of Hyperbilirubinemia in the Newborn Infant 35 or More Weeks of Gestation.," 2004), as well as the 2009 update, identify haemolysis as a major risk factor for hyperbilirubinemia and neurotoxicity. Haemolytic jaundice is likely when predischarge serum total bilirubin (STB) or transcutaneous bilirubin (TcB) levels fall within the high-risk zone on the hour-specific bilirubin nomogram (Bhutani et al., 2016), or when jaundice develops within the first 24 hours after birth. The most common causes of haemolysis include iso-immune haemolytic disease, which arises from blood group incompatibility and is associated with a positive direct anti-globulin test (or direct Coombs' test), glucose-6-phosphate dehydrogenase (G-6-PD) deficiency, and hereditary spherocytosis.

Liver-related Jaundice

Intrahepatic Causes

Chronic alcohol consumption can cause a variety of liver diseases, ranging from fatty liver with no symptoms to severe alcoholic hepatitis with jaundice, and finally cirrhosis with probable liver failure (Seitz et al., 2018). Jaundice in alcoholic liver illness can be caused by alcohol metabolites directly damaging cells or by decreased bile acid transport, which leads to cholestasis (Rocco et al., 2014). Around 30-40% of people with non-alcoholic fatty liver disease (NAFLD) advance to non-alcoholic steatohepatitis (NASH), with 40-50% developing fibrosis or cirrhosis, resulting in hyperbilirubinemia. Liver fat gain, particularly in type 2 diabetes, can cause inflammation and fibrosis (Byrne & Targher, 2015).

Sepsis can cause hyperbilirubinemia by disrupting BR transport and resulting in cholestasis (Ghenu et al., 2022). Drug-induced liver damage might be caused by direct toxicity or immunological activation, which causes inflammation and impaired BR transport (Chen et al., 2015). Wilson disease is a rare hereditary syndrome that affects copper transport in the liver, resulting in steatosis and cholestasis (Boskabadi et al., 2020). Other intrahepatic causes include autoimmune diseases such as autoimmune hepatitis and primary biliary cirrhosis, both of which produce inflammation and impede BR transport (Fargo et al., 2017).

Extrahepatic Causes

Conjugated hyperbilirubinemia can be a result of blockage in the bile duct outside the liver. The most prevalent benign cause of biliary blockage is choledocholithiasis, which accounts for 14% of new jaundice episodes (Fargo et al., 2017). Gallstones can obstruct the bile duct, resulting in jaundice or biliary strictures (Barreto & Windsor, 2018). In rare circumstances, gallbladder or cystic duct stones might compress the common hepatic duct or form a biliary-vascular fistula, both of which cause jaundice (Luu & Deziel, 2014). Postoperative jaundice is rare following cholecystectomy (0.6% of cases) (diagnostic approaches to the patient with jaundice), although operations such as liver transplants or the Whipple surgery can also result in biliary strictures. Chronic pancreatitis and cholangitis might cause similar symptoms (Barreto & Windsor, 2018). Biliary atresia or choledochal cysts are the main cause of extrahepatic jaundice in children.

Malignancies also contribute to new cases of jaundice. Although rare, gallbladder cancer is the most common cancer of the biliary system, with risk factors including gallstones, *Salmonella typhi* infection, and female sex. Additionally, ampullary tumors, lymphadenopathy, and external malignancies such as pancreatic cancer can obstruct the bile ducts, leading to jaundice.

Genetic Causes

Gilbert syndrome, or benign hyperbilirubinemia, is characterized by a mild reduction in UGT1A1 enzyme activity, resulting in elevated serum BR levels ranging from 1 to 5 mg/dL (17–86 μmol/L) (Ukibe et al., 2024). Factors such as stress, fasting, and illness can further increase BR levels (Creeden et al., 2021).

Genetics and Familial Risk

Infants with siblings who have jaundice are more likely to get it, especially if it is treated. Infants with genetic abnormalities affecting BR metabolism, as well as those with G-6-PD deficiency or other hereditary haemolytic anaemias, are also at increased risk. Certain genetic combinations might increase jaundice, and some maternal herbal medicines can exacerbate it even worse (Gazzin et al., 2017).

Environmental Causes

Although genetics and underlying health issues are the leading causes of jaundice, some environmental variables can significantly raise the risk, particularly when liver function is impaired. The liver is essential for detoxifying toxic substances, but prolonged or excessive exposure to environmental toxins such as industrial chemicals, alcohol, narcotics, and recreational substances can limit its capacity to operate, potentially resulting in jaundice. While most drugs save lives, some might cause liver harm if not correctly processed. Another prevalent cause of jaundice is drug-induced liver damage (DLI) (Garcia-Cortes et al., 2020). Infections can also cause inflammation, damage, or blockages in the liver, which increases the risk of jaundice. Finally, a correct diet is critical for maintaining liver health. Poor nutrition can cause liver disorders, such as malnutrition, fatty liver, and obesity, which can increase the risk of jaundice.

Symptoms of Jaundice

Key Symptoms

The basic symptoms of jaundice are yellowing of the skin, sclera, and mucus membranes (Pan & Rivas, 2017), as indicated by the name,

which means yellow. Jaundice becomes noticeable in pale-skinned new-borns when BR levels reach 90 mmol/L. It is more difficult to detect in darker-skinned new-borns; thus, an examination of the sclera is necessary (Rehermann, 2016). It can also show other symptoms specific to the underlying conditions (Santos Silva et al., 2017).

Disease-Specific Symptoms

- Patients with haemolytic jaundice show anaemia, yellow skin and sclera, black urine, and high BR levels (Markovic et al., 2022).
- Patients with Hepatic jaundice present with abdominal pain, fever, vomiting, and nausea, as well as complications such as satiety, gastrointestinal bleeding, diarrhoea, anaemia, oedema, weight loss, and weakness (Abbas et al., 2016).
- Obstructive jaundice can appear as dark urine, pale faeces, and widespread itching. Obstructive jaundice can be identified by symptoms such as fever, biliary colic, weight loss, abdominal discomfort, or abdominal mass (Vagholkar, 2020).

Clinical Examination

BR skin staining in neonates can serve as a clinical reference to evaluate the degree of jaundice, which spreads from head to toe (Karim et al., 2023). Assess the infant under bright light, gently pressing the skin to evaluate its coloration. Pay particular attention to any yellowing that extends beyond the thighs, as this may indicate the need for immediate BR testing. For dark-skinned new-borns and those undergoing phototherapy, clinical evaluation is less accurate (Candel-Pau et al., 2024). Other methods to diagnose jaundice include:

Non-Invasive Methods

- Transcutaneous bilirubin (TcB) measurement: BR levels can be determined using non-invasive methods (Hussain et al., 2017). Transcutaneous bilirubin (TcB) measurement is a non-invasive technique used to assess serum BR levels. This method, known as transcutaneous bilirubinometry, functions by emitting light into the skin and analysing the intensity of the reflected wavelengths (Okwundu et al., 2023).
- Bilimeter: This spectrophotometry-based approach measures total serum BR, which is especially useful in new-borns due to their high-unconjugated BR levels.

Invasive Methods

- Biochemical Method: The van den Bergh reaction and High-Pressure Liquid Chromatography (HPLC) are the invasive methods for determining BR levels. These techniques offer the highest level of accuracy but carry potential complications, including infection from inadequate sterilization, anaemia from repeated blood draws, and pain and distress caused by the frequent sampling required for continuous monitoring (Dzulkifli et al., 2018).

Parental Precautions for Physiological Jaundice

The parents should be informed about the benign nature of jaundice. The mother should be urged to breastfeed her new-born frequently and exclusively, at least eight to twelve times daily for the first few days without additional feeds or glucose water (Westerfield et al., 2018). If the baby's legs appear as yellow as his face, the mother should take him to the hospital. Any infant released before 48 hours of life should be assessed again within 48 hours for breastfeeding adequacy and the development of jaundice (Rite Gracia et al., 2017)

Management of Pathological Jaundice

Infants with yellow skin outside of the thighs should have their serum BR levels confirmed. Jaundice developing within 24 hours should be treated as haemolytic jaundice. Treatment is based on the type of BR build-up (conjugated, unconjugated) and may include phototherapy (standard, intense, or exchange transfusion), exchange transfusion, intravenous immunoglobulin, and follow-up care.

Treatment for Unconjugated Hyperbilirubinemia

Phototherapy

Phototherapy is a very successful and less intrusive treatment for hyperbilirubinemia (Patel et al., 2024). Its success is dependent on elements such as exposed surface area light spectrum, and irradiance. Phototherapy with two surfaces is more effective than phototherapy with only one. Special blue lights (F20T12/BB) are favoured over F20T12/B lights, and keeping the new-born 15-20 cm away from the light improves efficacy. Continuous phototherapy suggested, with breaks only for feeding and diaper changes.

- Conventional phototherapy is appropriate for non-haemolytic or slowly developing jaundice.
- Intensive phototherapies treat haemolytic jaundice or a fast rise in BR. It uses high spectrum irradiance (≥30 $\mu W/cm^2/nm$) to treat infant jaundice and specific skin diseases. Its effectiveness is dependent on light wavelength, irradiance, and overall exposure. It reduces BR levels in infants more effectively than standard phototherapy. Irradiance must be precisely measured and monitored to assure both safety and therapeutic efficacy (Patel et al., 2024).

These examinations identify any haemolytic aetiology of jaundice. Phototherapy considered unsuccessful if it fails to lower BR levels by 1–2 mg/dL within 4–6 hours or to keep BR levels below the threshold for exchange transfusion. However, regardless of BR level, an exchange transfusion (ET) may be undertaken if there is any concern regarding BR encephalopathy (Qian et al., 2022).

Exchange Therapy

Exchange transfusion is a key treatment for severe unconjugated hyperbilirubinemia, particularly when phototherapy is ineffective or TSB levels fall within the exchange threshold. This procedure rapidly lowers BR, removes haemolysis by-products, and clears circulating antibodies.

During a double-volume exchange, the neonate's blood is replaced with cross-matched donor blood. As BR redistributes from extravascular stores, TSB levels initially drop to 60% of pre-exchange values, later rising to 70–80%.

Closely monitor vital signs throughout the procedure. Assessment of Post-transfusion, TSB, CBC, serum calcium, glucose, and electrolytes should be done. Potential complications include thrombocytopenia, arrhythmias, infections, graft-versus-host disease, necrotizing enterocolitis, and electrolyte imbalances. Phototherapy should continue after the transfusion until BR reaches a safe level (Issa et al., 2024)

Intravenous Immunoglobulin

IVIG is used to treat unconjugated hyperbilirubinemia induced by immune-mediated haemolysis. It operates by preventing RBC degradation via Fc receptor blockage. If TSB levels remain within 2-3 mg/dL of the exchange threshold with extensive phototherapy, IVIG infusion is suggested. Although there is limited evidence to support IVIG's utility in lowering the need for exchange transfusions, it is still used in clinical practice to treat unconjugated hyperbilirubinemia (Vardar et al., 2022).

Treatment for Conjugated Hyperbilirubinemia

The treatment for conjugated hyperbilirubinemia varies according to the underlying cause. Biliary atresia is the most prevalent surgically correctable liver disease, accounting for a sizable proportion of babies admitted to hepatobiliary facilities. Early in life, one-third of afflicted new-borns may have normal-coloured faeces due to temporarily patent bile ducts. As atresia advances, bile flow stops, resulting in pale, chalky faeces. A hepatic portoenterostomy (Kasai surgery) performed in children less than 3 months old produces the best results (Wong & Wong, 2017). This procedure removes atretic bile ducts and fibrous tissue, resulting in a new biliary drainage channel via a Roux-en-Y anastomosis with the jejunum (Islek & Tumgor, 2022).

Antimicrobials are used for the management of infectious cholestasis, while bile acid synthesis disorders (BASDs) often respond to treatment with cholic and chenodeoxycholic acids. Metabolic cholestasis generally improves with underlying condition treatment. For neonatal hemochromatosis (GALD), IVIG and double-volume exchange transfusion are effective therapeutic options. Although liver transplantation offers a definitive cure, it remains technically challenging in this age group. In cases of parenteral nutrition (PN)-induced cholestasis, cyclic PN helps minimize exposure, and initiate enteral feeding as early as possible. Reducing manganese and copper levels in PN formulations can also help protect against liver damage.

At 3 months of corrected age, new-borns with serum BR ≥20 mg/dl or requiring exchange transfusion should have a neurodevelopmental follow-up (Elmazzahy et al., 2024) and a hearing examination (BAER) performed.

Conclusion

Jaundice in children, particularly new-borns, is a widespread condition primarily caused by immature BR metabolism or underlying pathological factors such as haemolysis, liver dysfunction, or biliary obstruction. While most cases resolve naturally, severe hyperbilirubinemia can lead to complications like kernicterus or long-term neurological damage. Early diagnosis through clinical examination and BR measurement is critical for distinguishing between physiological and pathological jaundice. Management strategies, including phototherapy, exchange transfusion, and pharmacological treatments, tailored to the specific cause. Parental education and timely follow-up play a key role in ensuring optimal outcomes and minimizing long-term risks associated with untreated or severe jaundice.

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