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NEONATAL JAUNDICE: AN OVERVIEW

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ABSTRACT: When an infant has a high level of bilirubin in the blood, it develops newborn jaundice. The body produces bilirubin, a yellow material, as it replaces worn-out red blood cells. The material is broken down by the liver so that it can be eliminated from the body through stools. Because of physiological jaundice or breastfeeding, neonatal jaundice is frequent and typically harmless. 80% of healthy newborns have some degree of hyperbilirubinemia at birth, although only 5–10% of them need treatment to avoid harm or address the underlying cause of jaundice. Neonatal jaundice can be classified as conjugated and unconjugated and can have several causes such as breast milk feeding, blood group incompatibility, hemolysis, or genetic defects of enzymes in the bilirubin metabolism pathway. Although in some severe situations, long-term effects can become severe and irreversible. Early diagnosis and treatment are so crucial. Phototherapy, intravenous immunoglobulins, and exchange transfusions can all be used to treat severe cases of neonatal jaundice. This activity reviews the etiology, epidemiology, pathophysiology, diagnosis, and management of neonatal jaundice.

***Keywords*:** Neonatal Jaundice, Phototherapy, Bilirubinometer

INTRODUCTION:

Neonatal jaundice or neonatal hyperbilirubinemia results from elevated total serum bilirubin (TSB) and clinically manifests as yellowish discoloration of the skin, sclera, and mucous membrane. The term jaundice derives from the French word "Jaune," which means yellow. It is the most commonly encountered medical problem in the first two weeks of life and a common cause of readmission to the hospital after birth[1]. In most infants, an increase in bilirubin production (e.g., due to hemolysis) is the primary cause of severe hyperbilirubinemia, and thus reducing bilirubin production is a rational approach for its management[2]. Approximately 60% of term and 80% of preterm newborns develop clinical jaundice in the first week after birth[3]. The situation can become critical in infants with an associated impaired bilirubin elimination mechanism as a result of a genetic deficiency and/or polymorphism[2]. According to National Neonatal-Perinatal Database (NNPD), the incidence of neonatal hyperbilirubinemia in in-house live births is 3.3%, while in extramural admissions morbidity due to hyperbilirubinemia accounted for 22.1%[4].

In 2010, the inability to treat jaundice resulted in 114,000 avoidable infant deaths. Moreover, 75,000 children around the world are suffering from brain dysfunction due to jaundice complications. Hyperbilirubinemia is one of the top three causes of death among newborns, according to studies[5]. As bilirubin is toxic to the brain cells, acute bilirubin encephalopathy can occur in cases of extreme jaundice. This condition can result in brain trauma and lead to kernicterus, which causes repetitive and uncontrolled movements, a permanent upward look, and hearing loss. However, timely treatment can help in preventing long-term damage[6]. Neonatal jaundice is categorized into two groups: conjugated and unconjugated. A bilirubin level of more than 85 µmol/l (5mg/dL) leads to a jaundiced appearance in neonates whereas in adults a level of 34 µmol/l (2 mg/dL) is needed for this to occur. In newborns, jaundice is detected by blanching the skin with pressure applied by a finger so that it reveals underlying skin and subcutaneous tissue[7]. Infants whose palms and soles are yellow have serum bilirubin levels over 255 µmol/l (15 mg/dL) (more serious level)[8]. Diagnosis is often by measuring the serum bilirubin level in the blood. In those who are born after 35 weeks and are more than a day old transcutaneous bilirubinometer may also be used[9]. Jaundice can be treated with phototherapy, which can be further split into conventional, intense and exchange transfusions, as well as pharmacological treatment, which can be further divided into phenobarbitone, intravenous immunoglobulins (IVIG), metalloporphyrins, and follow-up medications[10]. However, any newborn with total serum bilirubin greater than 359 µmol/l (21 mg/dL) should receive phototherapy[11].

Jaundice in Newborns

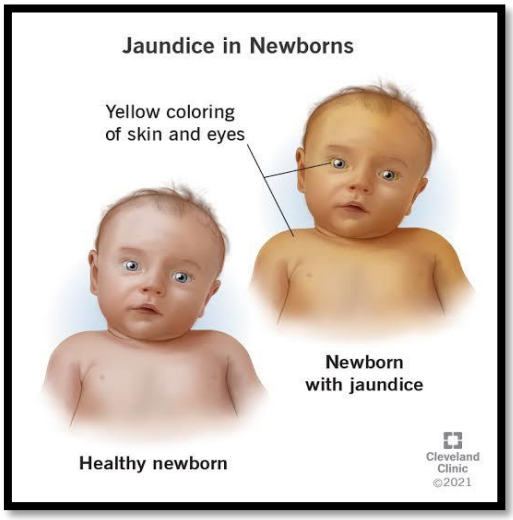


Fig.1 Jaundice in Newborns[78]

ETIOLOGY:

There are two distinct types of Neonatal hyperbilirubinemia:

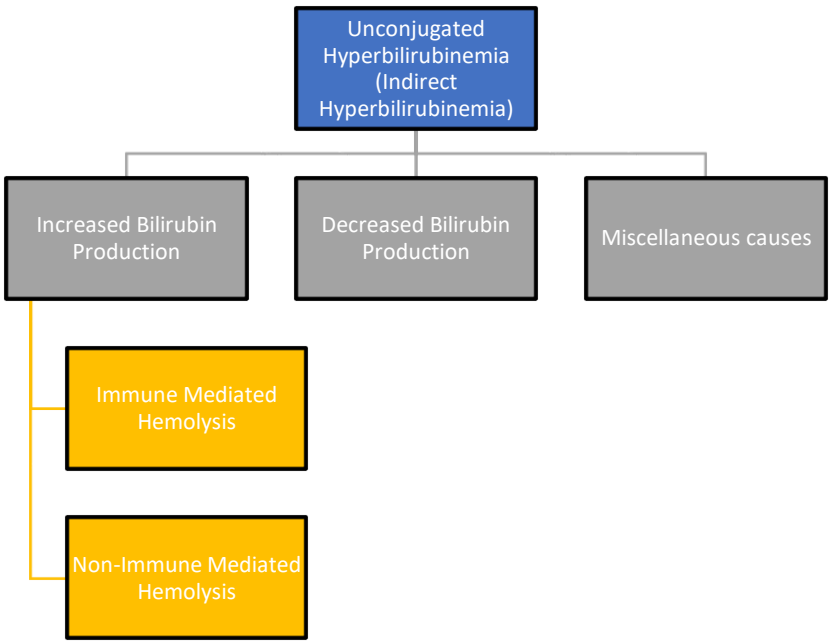
Unconjugated Hyperbilirubinemia (UHB) or Indirect Hyperbilirubinemia

Unconjugated hyperbilirubinemia is the more common type and is either physiological or pathological. 75% of neonatal hyperbilirubinemia is caused by physiological jaundice, which is caused by a change in the way that newborn bilirubin is processed physiologically. In contrast to newborns, who have biologically higher TSB levels, healthy adults often have TSB levels of less than 1mg/dl[12]. Physiological jaundice typically appears after 24 hours of age, peaks at around 48-96 hours, and resolves by two to three weeks in full-term infants[13].

Jaundice is deemed pathological if it appears on the first day of birth, TSB is higher than the 95th percentile for age based on age-specific bilirubin nomograms, levels rise by more than 5 mg/dL/day or more than 0.2 mg/hr, or jaundice continues for longer than 2 to 3 weeks in full-term infants[11].

The etiology of unconjugated hyperbilirubinemia can be classified into the following three groups based on the mechanism of bilirubin elevation:

Classification of Unconjugated Hyperbilirubinemia



Classification of Unconjugated Hyperbilirubinemia

1: Increased Bilirubin Production

Immune-mediated hemolysis - Includes blood group incompatibilities such as ABO and Rhesus incompatibility.

Non-immune mediated hemolysis is caused by conditions such as polycythemia, sepsis, and RBC membrane defects such as hereditary spherocytosis and elliptocytosis, as well as RBC enzyme deficiencies such as glucose-6-phosphate dehydrogenase (G6PD) deficiency and pyruvate kinase deficiency[14].

2: Decreased Bilirubin Clearance

Crigler-Najjar type I & II, and Gilbert syndrome[14].

3: **Miscellaneous Causes**

Other diverse etiologies include the infant of a diabetic mother, congenital hypothyroidism, medications such as ceftriaxone, penicillins, and sulfa medicines, intestinal blockage, pyloric stenosis, breast milk jaundice, and breastfeeding jaundice[14].

Increased Bilirubin Production:

Immune-mediated hemolysis

Exaggerated hemolysis:

The most frequent cause of pathological hyperbilirubinemia in infants is exaggerated hemolysis, whether immunological or non-immune caused. Newborn hemolytic illness is caused by immune-mediated hemolysis, which is found with blood type incompatibility such as ABO/RH incompatibility (HDN). Preformed maternal anti-A and anti-B antibodies of the immunoglobulin (Ig) G subclass enter the placenta in HDN due to ABO incompatibility, resulting in hemolysis and UHB in babies with blood types A, B, or AB. The direct Coombs test is used to aid in the diagnosis, but it has a limited positive predictive value and sensitivity for severe UHB[15]. ABO incompatibility between mother and fetus exists in about 15% of pregnancies, but HDN due to ABO incompatibility is seen only in 4% of newborns with ABO incompatibility[16].

Rhesus (Rh) incompatibility:

Rhesus (Rh) incompatibility occurs when an Rh-negative mother, who has previously been exposed to Rh-positive RBCs, typically from a prior pregnancy or miscarriage, gets sensitized and produces antibodies against the Rh antigen. Initial IgM antibodies produced by sensitization are unable to cross the placenta. But in later pregnancies, the transition in antibody class results in IgG antibodies that can cross the placenta and cause RBC hemolysis in the fetus with Rh-positive blood. As a result of the Rh antigen's high immunogenicity, HDN that results from it is typically severe and frequently causes hydrops in fetuses or severe UHB in neonates. The American College of Obstetricians and Gynecologists (ACOG) has advised that all Rh-negative expectant mothers get anti-D immune globulin at 28 weeks of pregnancy and once more after delivery if the baby is Rh-positive or undetermined[17].

Non-immune causes of UHB:

Non-immune causes of UHB include RBC enzyme defects, RBC membrane defects, hemoglobinopathies, sepsis, sequestration, and polycythemia.

- RBC enzyme defects

  The most prevalent RBC enzyme defect is the glucose-6 phosphatase dehydrogenase (G6PD) enzyme deficit, which is passed on as an X-linked recessive condition. By converting NADP into NADPH (nicotinamide adenine dinucleotide phosphate hydrogenase), G6PD guards RBCs against oxidative damage (nicotinamide adenine dinucleotide phosphate). G6PD-deficient RBCs are hemolyzed and lead to anemia and hyperbilirubinemia when exposed to oxidant stressors like disease, certain drugs, colors, and foods like fava beans. It is known that more than 200 different kinds of mutations can result in G6PD deficiency[18].

  Pyruvate kinase deficiency (PKD) is another enzyme deficiency that causes hemolysis and may present as UHB in newborns. It is an autosomal recessive (AR) condition brought on by a problem with the machinery that produces ATP. RBCs, particularly youthful RBCs, have a shorter life span in PKD, which causes anemia and UHB[19].
- UHB due to RBC membrane defects

  UHB due to RBC membrane defects includes hereditary spherocytosis (HS) and hereditary elliptocytosis (HE). HS, also known as Minkowski Chauffard disease, is the most common RBC membrane defect caused by mutations in RBC membrane proteins[20]. Most cases are transmitted as an autosomal dominant (AD) trait and can present in the neonatal period with UHB[21].

  Hereditary elliptocytosis is another type of RBC membrane defect that is mostly asymptomatic but rarely does cause UHB in the neonatal period[22].
- RBC sequestrations

  Due to increased bilirubin burden, RBC sequestrations from cephalohematoma, subgaleal hemorrhage, and intracranial hemorrhage are all significant causes or risk factors for UHB in the neonatal period. Another condition linked to a higher risk of UHB in newborns is polycythemia[23].

Decreased Bilirubin Clearance:

- Gilbert syndrome

  Gilbert syndrome is the most common of these and results from a mutation in the UGT1A1 gene resulting in decreased UGT production leading to unconjugated hyperbilirubinemia[24]. When under stress and without hemolysis or liver damage, Gilbert syndrome often manifests as moderate jaundice[25].
- Crigler-Najjar syndrome

A total lack of UGT activity causes Crigler-Najjar syndrome type 1, an AR disease. Patients with the condition commonly develop bilirubin encephalopathy after presenting with significant hyperbilirubinemia in the first few days of life. Some of the activity of UGT enzymes is still present in people with Crigler-Najjar syndrome type 2. Due to this, TSB levels are not excessive and bilirubin encephalopathy in patients is uncommon[26].

Miscellaneous Causes:

- Breastfeeding jaundice

  Breastfeeding jaundice (or "lack of breastfeeding jaundice") is caused by insufficient breast milk intake[27]. This results in inadequate quantities of bowel movements to remove bilirubin from the body. This leads to increased enterohepatic circulation, resulting in increased reabsorption of bilirubin from the intestines[28]. Most cases can be alleviated by regular nursing sessions that are long enough to induce enough milk supply, which typically occurs in the first week of life[29].
- Breast milk jaundice

  Jaundice brought on by breast milk starts late in the first week, peaks in the second, and normally goes away by two weeks of age. It is believed that the primary causes are the inhibition of the UGT enzyme by pregnanediol and the intestinal deconjugation of conjugated bilirubin by the beta-glucuronidase found in breast milk[30].
- Other miscellaneous causes of UHB

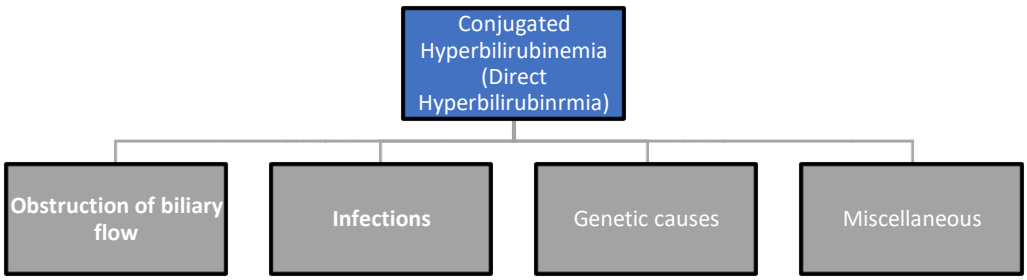
  It includes IDM, gastrointestinal obstruction, congenital hypothyroidism, and certain medications[14].

Conjugated Hyperbilirubinemia (CHB) or Direct Hyperbilirubinemia

Conjugated hyperbilirubinemia, also referred to as neonatal cholestasis, is characterized by the elevation of serum conjugated/direct) bilirubin (> 1.0 mg/dL) and is due to impaired hepatobiliary function[14].

The etiology of conjugated hyperbilirubinemia can be classified into the following four groups based on the mechanism of bilirubin elevation:

Classification of Conjugated Hyperbilirubinemia



Classification of Conjugated Hyperbilirubinemia

1. **Obstruction of biliary flow:**

   Biliary atresia, choledochal cysts, neonatal sclerosing cholangitis, neonatal cholelithiasis.

2. **Infections:**

   CMV, HIV, rubella, herpes virus, syphilis, toxoplasmosis, urinary tract infection (UTI), septicemia

3. **Genetic causes**:

   Alagille syndrome, alpha-1 antitrypsin deficiency, galactosemia, fructosemia, Tyrosinemia type 1, cystic fibrosis, progressive familial intrahepatic cholestasis (PFIC), Aagenaes syndrome, Dubin-Johnson syndrome, Bile acid synthesis disorders(BSAD)

4. **Miscellaneous:**

   Idiopathic neonatal hepatitis, parenteral nutrition-induced cholestasis, gestational alloimmune liver disease/neonatal hemochromatosis, hypotension[14].

Obstruction of biliary flow:

- Biliary atresia (BA)

  Biliary atresia (BA) is the most common cause of conjugated hyperbilirubinemia in infants[31]. The etiology of BA is not well understood, but genetic factors along with viral infection, toxins, chronic inflammatory and autoimmune

injury to bile ducts seem to play a role in its pathogenesis. The disease involves both intra-hepatic and extra-hepatic bile ducts and classically presents around 2 to 4 weeks of life with pale stools and jaundice[32].

- Choledochal cysts

  Choledochal cysts involve dilation of the intrahepatic and extra-hepatic bile ducts. Unlike sclerosed ducts in biliary atresia, cysts with normal or dilated intrahepatic bile ducts can be found by ultrasound. Cystic biliary atresia, however, resembles choledochal cysts in some cases[33]

Infections:

- Cytomegalovirus (CMV)

  Cytomegalovirus (CMV) is the most common congenital infection that manifests in various ways. The majority of infected neonates are asymptomatic, although the most obvious signs of hepatic involvement are hepatomegaly and CHB[34].

Genetic causes:

Galactosemia, fructosemia, and tyrosinemia type 1 are a few of the inborn errors of metabolism known to cause cholestasis in neonates.

- Galactose-1-phosphate uridyl transferase (GALT)

  A lack of galactose-1-phosphate uridyl transferase (GALT) causes harmful galactose metabolites to build up in many organs. Galactosemia is diagnosed based on the presence of reducing chemicals in the urine and GALT activity in the liver or erythrocytes[14].
- Bile acid synthesis disorder (BASD)

  A lack of one of the enzymes necessary to produce bile acids from cholesterol causes bile acid synthesis disorder (BASD). Although BASDs is a rare cause of cholestasis, many of them can be treated with just medical care[14].

Miscellaneous:

- Parenteral nutrition-associated cholestasis (PNAC)

  Most frequently seen in premature infants receiving parenteral nourishment, parenteral nutrition-associated cholestasis (PNAC) is a significant iatrogenic cause of cholestasis (PN). Twenty percent of newborns who have received PN for longer than two weeks develop PNAC[35].
- Gestational alloimmune liver disease (GALD)

  Almost all cases of newborn hemochromatosis are caused by gestational alloimmune liver disease (GALD), a fulminant alloimmune illness that leads to liver failure from intra- and extra-hepatic iron accumulation[36].

EPIDEMIOLOGY:

Neonatal jaundice affects 60% of full-term infants and 80% of preterm infants in the first three days after birth. Although transient, the condition accounts for up to 75% of hospital readmissions in the first week after birth[37]. Geographical location and ethnicity affect incidence. Africans have a lower incidence than East Asians and American Indians. Greeks who reside in Greece are more common than Greeks of Greek heritage who reside outside of Greece. Incidence is higher in populations living at high altitudes. In 1984, 32.7% of infants with serum bilirubin levels of more than 205 µmol/L (12 mg/dL) at 3100 m of altitude[38]. Neonatal jaundice is more common in infants of American Indian, East Asian, and Greek ethnicity, however, the latter appears to solely apply to children born in Greece and may thus have environmental rather than ethnic roots. Compared to non-African infants, African infants are less frequently afflicted. Due to this, severe jaundice in a newborn from an African country justifies a closer examination of the causes, including G-6-PD deficiency. In 1985, Linn et al reported on a series in which 49% of East Asian, 20% of white, and 12% of black infants had serum bilirubin levels of more than 170 µmol/L (10 mg/dL)[39]. The risk of developing significant neonatal jaundice is higher in male infants. This does not appear to be related to bilirubin production rates, which are similar to those in female infants. The risk of significant neonatal jaundice is inversely proportional to gestational age[40]. While chronic bilirubin encephalopathy is less common, with an estimated incidence of 1 in 50,000 to 100,000 live births, acute bilirubin encephalopathy is reported at a rate of about 1 in 10,000 live births[41]. Compared to UCH, conjugated hyperbilirubinemia is far less frequent, occurring in about 1 in 2500 term newborns[42]. It is estimated that 60% to 70% of patients with biliary atresia (BA) will eventually require liver transplantation in childhood, and BA remains the most common indication for a pediatric liver transplant[43].

PATHOPHYSIOLOGY:

Jaundice is the yellow discoloration of skin, sclera, and mucous membrane which occurs due to the accumulation of unconjugated, lipid-soluble bilirubin pigment in the skin. It occurs in newborns because fetal erythrocytes are breaking down more often, shortening life expectancy. Additionally, newborns have a limited hepatic excretory capacity. These are more common in preterm infants than in term infants. Another often encountered type is breast milk jaundice, which develops when a mother's breast milk has specific components that boost enterohepatic circulation and, as a result, boost bilirubin production. In addition to these factors, blood type incompatibility and sepsis frequently result in jaundice becoming more severe because they enhance hemolysis, which in turn increases bilirubin production[44].

Neonatal jaundice may be a result of physiological or pathological mechanisms. The different mechanisms for the development of jaundice may be concluded into either an increase in bilirubin production, an increase in enterohepatic circulation, or a decrease in bilirubin elimination[45].

Bilirubin formation and metabolism:

As the byproduct of heme catabolism, bilirubin is created in the reticuloendothelial system and is created by oxidation-reduction reactions. The breakdown of myoglobin, cytochromes, and catalase are also involved in the production of bilirubin, which is obtained in around 75% of cases from hemoglobin[40]. Bilirubin is formed as a breakdown product of haem. In phagocytic cells of the reticuloendothelial system, the action of haem oxygenase opens up the tetrapyrrole ring of haem to produce biliverdin and carbon monoxide. Biliverdin is then reduced to bilirubin by biliverdin reductase[46].

Metabolism of haem to form bilirubin

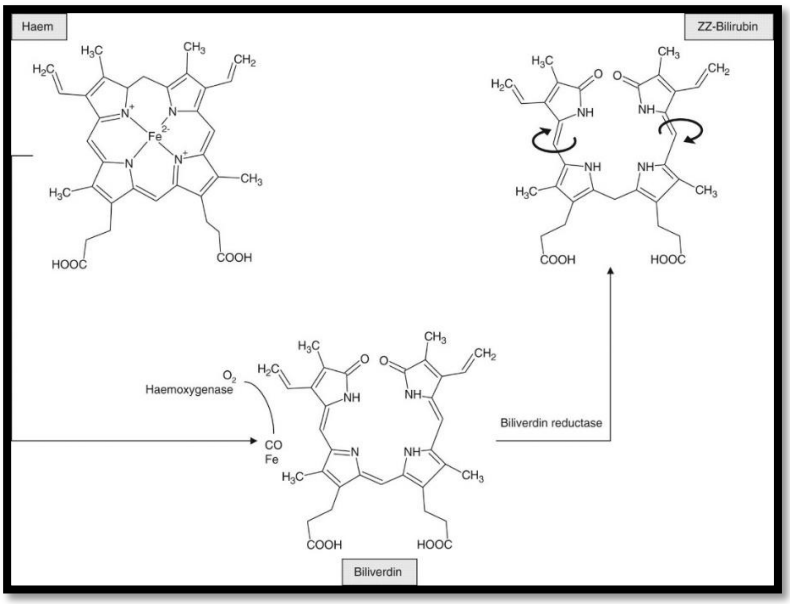


Fig.2 Metabolism of haem to form bilirubin[46]

Unconjugated bilirubin is hydrophobic and is carried to the liver in the bloodstream attached to albumin. There, it is converted to conjugated bilirubin by the enzyme uridine diphosphate-glucuronosyltransferase in the smooth endoplasmic reticulum (UGT).

Conjugated bilirubin is water-soluble, and after being broken down by intestinal bacterial flora, it is subsequently expelled in bile and into the GI tract, where it is primarily eliminated in feces. With the help of beta-glucuronidase, some conjugated bilirubin is partially deconjugated in the GI tract and reabsorbed via the enterohepatic circulation [47].

Increased understanding of the biochemical pathways involved has brought out not only the identification of the precise defect in the rare inherited hyperbilirubinemias but also the realization that certain groups of infants are more likely to suffer from neonatal jaundice than others [46].

DIAGNOSIS:

Diagnosis is often by measuring the serum bilirubin level in the blood. Transcutaneous bilirubinometers may also be used on newborns who were born beyond 35 weeks and were greater than a day old. It is not advised to use an icterometer, which is a transparent plastic piece painted with five transverse strips of graduated yellow lines [48].

The baby will be checked for jaundice within 72 hours of being born during the newborn physical examination [49]**.** Tests to detect jaundice and measure bilirubin includes:

- Visual examination
- Bilirubin test
- Further test

Visual examination:

A visual examination will be performed on your infant to check for jaundice symptoms. They must take off their clothes during this so that their skin may be examined in well-lit conditions, ideally natural light. Additional items that could be examined include:

- The pupil of your infant's eyes
- Gums of your infant
- The color of your infant's feces or pee[49]

Bilirubin test:

The amount of bilirubin in your baby's blood will need to be examined if it is suspected that they have jaundice. You can accomplish this by using:

- a tiny instrument known as a bilirubinometer shines a light on your infant's skin (it calculates the level of bilirubin by analyzing how the light reflects off or is absorbed by the skin)
- a blood examination using a sample of blood drawn by puncturing your infant's heel with a needle (the level of bilirubin in the liquid part of the blood called the serum is then measured)

A bilirubinometer is typically used to test for jaundice in infants.

Blood tests are often only required if your infant acquired jaundice within 24 hours of birth or the reading is unusually high. Whether or whether your infant needs treatment depends on the amount of bilirubin found in their blood[49].

Bilirubinometer- Jaundice meter

Fig.3 Bilirubinometer- Jaundice meter[50]

Further test:

Further blood tests may be needed if your baby's jaundice lasts longer than 2 weeks or if treatment is needed. The blood is examined to establish:

- The blood type of the infant (to determine whether it is incompatible with the mother)
- If the baby's red blood cells have any antibodies (infection-fighting proteins) bound to them
- The number of cells in the baby's blood
- If there is an infection
- Whether there's an enzyme deficiency
- These tests assist in identifying any underlying conditions that may be causing elevated bilirubin levels[49].

When treating newborn cholestasis, radiology is frequently required. Gallstones, inspissated bile, choledochal cysts, and sludge in the biliary tree may all be detectable using hepatic ultrasonography. On hepatic ultrasound, the triangular cord sign has high sensitivity and a nearly perfect specificity for biliary atresia[51].

Additional tests like TORCH titers, urine cultures, viral cultures, serologic titers, Newborn screening results, specific tests for inborn errors of metabolism, alpha-1 antitrypsin phenotype, and specific genetics tests may be needed depending on the scenario[14]. It has been demonstrated that phenobarbitone therapy beforehand increases the sensitivity of this imaging. And finally, liver biopsy is typically regarded as the gold standard for cholestasis in newborns. In 90% to 95% of cases, a competent pathologist's interpretation of the histopathology will aid in making an accurate diagnosis and may help patients with intrahepatic cholestasis avoid needless procedures[52].

TREATMENTS:

Tests must be performed to determine whether your infant has excessive amounts of a substance called bilirubin in their blood, as treatment is typically only required if this is the case. The majority of infants with jaundice do not require treatment since their blood bilirubin levels are reported to be low. In these situations, the problem often improves within 10 to 14 days and won't harm your kid[49].

Unconjugated hyperbilirubinemia

The two mainstays of treatment for patients with unconjugated hyperbilirubinemia are phototherapy and exchange transfusion[14].

1. **Phototherapy**:

Phototherapy is considered the safest intervention approach used in the treatment of neonatal jaundice. Regardless of the underlying reason, phototherapy was effective in reducing the amount of total serum bilirubin in all patients with newborn jaundice[53][54]. The amount of surface area exposed to phototherapy affects its effectiveness: Potentially more effective than single-surface phototherapy is double-surface phototherapy[55].

(a) Conventional Phototherapy

One can use conventional or fiber-optic phototherapy units provided jaundice is non-hemolytic or its progression is slow.

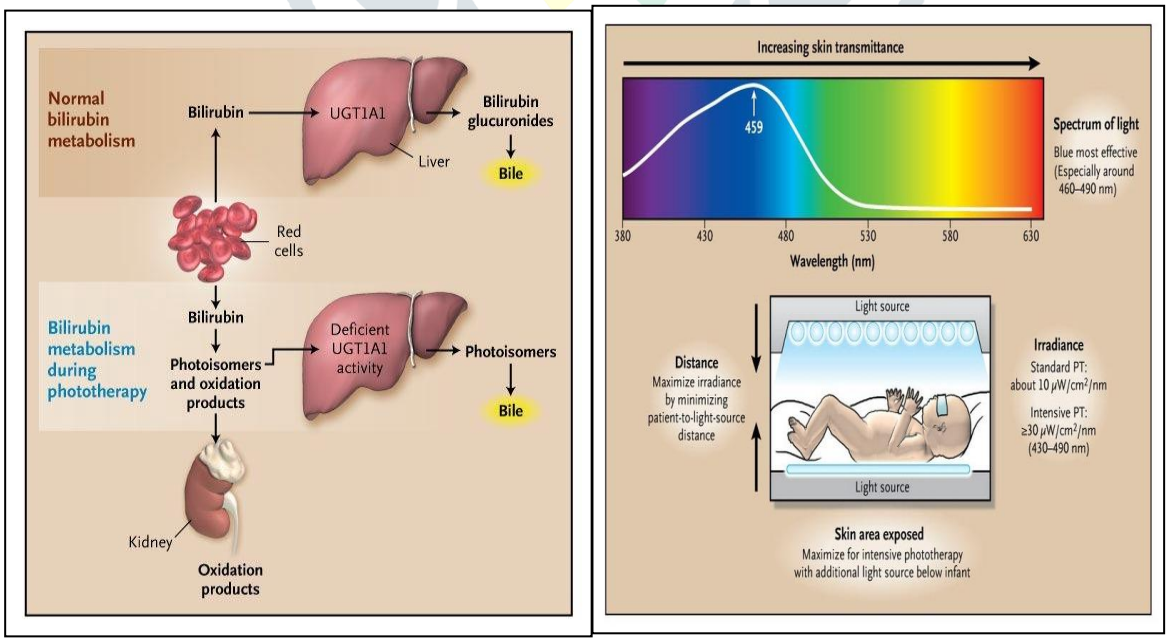
(b) Intensive Phototherapy

Utilizing intensive phototherapy is justified under conditions such as hemolytic jaundice, quickly rising bilirubin, or when a regular unit is ineffective. Two important treatments involve putting the infant on the bili-blanket, utilizing additional overhead phototherapy units that have blue lights, and reducing the phototherapy devices to a distance of 15-20 cm[56].

(c) Exchange Transfusion

Hemolytic antibodies and bilirubin are eliminated during exchange transfusions[57].

This can be accomplished by using light energy to alter the form and structure of bilirubin, allowing it to be transformed into molecules that can be excreted even when regular conjugation is inadequate[58]. A portion of the pigment is subjected to a succession of photochemical processes as a result of light absorption by dermal and subcutaneous bilirubin, each of which happens at a different rate. Bilirubin absorbs light most significantly in the blue region of the spectrum (near 460 nm). Light penetration through tissue in this region increases dramatically as the wavelength increases[59]. The amount and kind of light utilized have a big impact on how quickly bilirubin photoproducts form since only the wavelengths that are absorbed by bilirubin and penetrate tissue have a phototherapeutic effect. A light source that emits light in the 460–490 nm region of the spectrum is the most effective for treating hyperbilirubinemia when all of these criteria are taken into account (blue)[60]. Phototherapy as a treatment method for jaundice is safe, comfortable, and reliable. However, more invasive and dangerous treatments, such as exchange transfusion, are used to treat jaundiced children who do not react to phototherapy or who have high hyperbilirubinemia at the time of diagnosis. This is done to prevent or lessen bilirubin-induced brain damage[61]. The total serum bilirubin level increases after phototherapy are stopped, and this increase is referred to as "rebound bilirubin". Most of the time, the "rebound bilirubin" level is lower than the level at the phototherapy's start and does not necessitate restarting the treatment[62]. Few studies have also reported an increased incidence of solid organ tumors and non-lymphocytic leukemias in children treated with phototherapy[63][64]. Another frequently discussed phototherapy-related condition called the bronze infant syndrome causes uneven coloring of the skin, mucous membranes, and urine. It is frequently observed in newborns with increased serum levels of conjugated bilirubin. The exact mechanism is unknown, however, it seems to be connected to the deposition of biliverdin and photoisomers of bilirubin[65][66].



Phototherapy for Neonatal Jaundice

Fig.4 Phototherapy for Neonatal Jaundice[79]

2. **Exchange Transfusion:**

- Exchange transfusion became the second-line treatment when phototherapy failed to control serum bilirubin levels. However, research has shown that IVIG therapy can considerably lower the requirement for exchange transfusions in

newborns with Rh or ABO isoimmunization[67][68]. A complete blood transfusion sometimes referred to as an exchange transfusion, may be necessary if your infant has a very high blood bilirubin level or if phototherapy has not been successful[49]. The purpose of exchange transfusion is to remove bilirubin from the blood, particularly in infant patients who have acute bilirubin encephalopathy or kernicterus problems[69]. Exchange transfusion may have the following complications:

- Hemolytic reactions
- Infections
- Portal vein thrombosis
- Electrolyte disturbances
- Increase blood volume
- Iron overload[70]

Anemia (cord hemoglobin 11 g/dL), an increased cord bilirubin level (>70 mol/L or 4.5 mg/dL), or both are the most common reasons for early exchange transfusion. A moderate rate of increase (>8-10 mol/L/h or 0.5 mg/dL/h) in the presence of moderate anemia (11-13 g/dL), as well as a rapid rate of increase in the serum bilirubin level (>15-20 mol/L /h or 1 mg/dL/h), were both indicators for exchange transfusion. Infants with hemolytic jaundice required an exchange transfusion when their serum bilirubin levels reached 350 mol/L (20 mg/dL) or increased at a rate that suggested they would reach this level or greater. The majority of medical professionals now advocate an individualized approach, acknowledging that exchange transfusion is not a risk-free procedure, that effective phototherapy converts 15–25% of bilirubin to nontoxic isomers, and that transfusion of a small volume of packed red blood cells may treat anemia[40].

Exchange Transfusion for Neonatal Jaundice

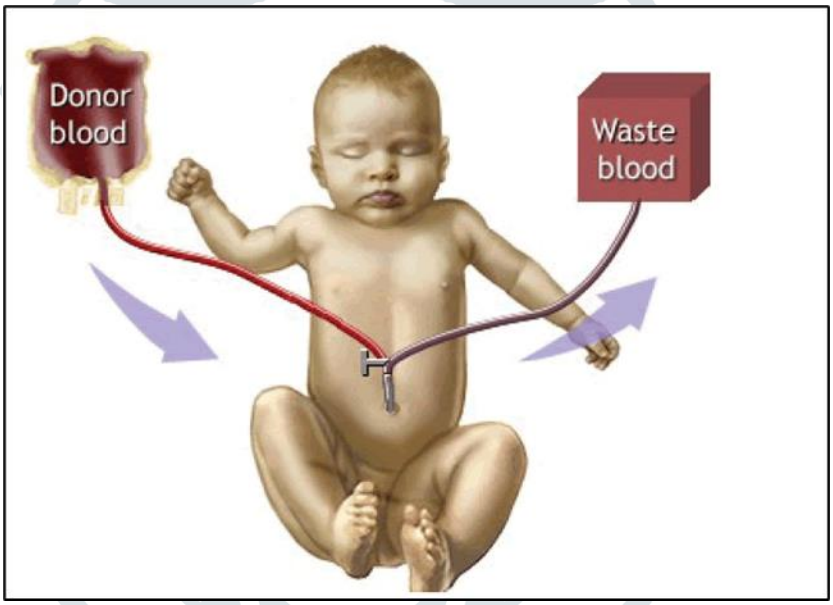


Fig5. Exchange Transfusion for Neonatal Jaundice[71]

3. Intravenous immunoglobulin:

Evidence-based, IVIG therapy for hemolytic disorders can reduce the requirement for exchange transfusions[73]. Intravenous gamma globulin has been shown to significantly reduce the need for exchange transfusion in ABO and Rh hemolytic disease[74]. The healing of the main condition and liver functioning will often have an impact on metabolic causes of cholestasis. IVIG and double-volume exchange transfusions seem to work effectively for patients with GALD. In this age group, liver transplantation is technically difficult yet curative when it is available[75].

Conjugated Hyperbilirubinemia:

Conjugated hyperbilirubinemia is treated according to the underlying cause. For the best results, patients with biliary atresia should have a Kasai procedure (hepatic portoenterostomy) as soon as possible after their diagnosis[72]. The Kasai operation involves removing the fibrous plate and atretic biliary channels, followed by Roux-en-Y anastomosis of the jejunum with the remaining ducts to create a different route for biliary drainage[76]. While treatment with cholic acid and chenodeoxycholic acid is frequently curative for many BASDs, treatment for infectious causes of cholestasis would be treated with particular anti-microbials. Typically, metabolic reasons for cholestasis would improve when the underlying condition and liver functioning did. IVIG and double-volume exchange transfusions seem to be effective treatments for GALD patients. When accessible, liver transplantation is curative but technically difficult in this age group[77]. Cyclical parenteral nutrition (PN) is used to treat cholestasis brought on by parenteral nutrition by shortening the exposure time and starting enteral feeds as soon as possible. To lessen liver damage, PN should have less manganese and copper[14].

CONCLUSION:

Neonatal Jaundice still contributes significantly to neonatal morbidity, mortality, and long-term handicap, especially in developing countries. This is made worse by ignorance on the part of parents and health workers which contributes to delays in seeking proper medical care. However, education at the Primary Health Care level, prompt diagnosis, and treatments include Phototherapy, Exchange Transfusion, Intravenous immunoglobulin, etc. from which Phototherapy is the most effective one. Referral to the appropriate specialist will go a long way to prevent jaundice-associated problems early so that death is averted and the child will have a good quality of life.

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