Madonna University Journal of Medicine and Health Sciences. Volume 2 issue 3(2022),Pp. 25-41© Madonna University Press,
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A SYSTEMATIC REVIEW ON PHYSIOLOGICAL JAUNDICE: DIAGNOSIS AND MANAGEMENT OF THE AFFECTED NEONATES

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ABSTRACT

Jaundice is the most common physical abnormality in the first week of life. Physiological jaundice is increase in the level of bilirubin in the blood which is not immunologically induced as seen in pathological jaundice caused by blood group incompatibility such as ABO or Rh blood groups. Physiological jaundice can be treated with phototherapy. This paper was written to give an insight into physiological jaundice. Many search engines such as Google scholar, Pubmed central, Web of Science, Scopus, Researchgate, Academia Edu, etc were searched for related information. Physiological jaundice can easily manged with exposure to sun light which metabolises the bilirubin.

Keywords*: jaundice, physiological jaundice, diagnosis, management, neonates*

INTRODUCTION

Jaundice is the most common physical abnormality in the first week of life. Her 25–50% of all term newborns and a higher proportion of preterm infants develop clinical jaundice (Dayama *et al.*, 2015; Obeagu, 2019).

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Jaundice is defined as yellowing of the skin, mucous membranes, and sclera due to the deposition of yellow-orange bile pigment. H. bilirubin (Muhammad et al., 2016).

Enzyme immaturity and limited substrate availability are temporary and normalize in the first few days of life.

In breastfed infants, prolonged unconjugated hyperbilirubinemia beyond the third week of life in healthy neonates is a normal and regularly occurring extension of physiologic jaundice. This is called breast milk jaundice. Human breast milk factors that may be associated with the etiology of breast milk jaundice include pregnane-3α, 20β-diol, interleukin IL1β, β-glucuronidase, epidermal growth factor, and α-fetoprotein (Stephanie B et al. 2021). Inadequate caloric intake due to maternal and/or infant breastfeeding problems can also increase serum levels of unconjugated bilirubin. 2021).

A newborn has a bilirubin formation rate two to three times higher than that of an adult, largely due to the high hematocrit and short life span of the newborn's red blood cells. Decreased bilirubin excretion is due to impaired ability of the neonatal liver to conjugate bilirubin and increased enterohepatic recirculation. Jaundice can result from an increase in either unconjugated (indirect) or conjugated (direct) bilirubin (Willy, 2021).

The use of anti-D immunoglobulin significantly reduced the incidence of jaundice due to Rh incompatibility. Hereditary hemolytic anemia, presenting as jaundice at birth, can lead to indirect hyperbilirubinemia and encephalopathy. Detection of neonatal hereditary hemolytic anemia is useful for early detection, treatment, and prevention (Dayama et al., 2015).

ETIOLOGY

Bilirubin is formed from the catabolism of heme. About 75% of bilirubin is derived from the breakdown of hemoglobin from aged red blood cells. The remainder results from ineffective

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erythropoiesis and the breakdown of heme proteins such as cytochromes, myoglobin, nitric oxide synthase, glutathione peroxidase, and catalase. There are two types of neonatal hyperbilirubinemia.

Type I: unconjugated hyperbilirubinemia (UHB) or indirect hyperbilirubinemia

Unconjugated hyperbilirubinemia is the more common type and can be physiological or pathological. Physiological jaundice accounts for 75% of neonatal hyperbilirubinemia and results from physiological alterations in neonatal bilirubin metabolism. Healthy adults have normal total serum bilirubin (TSB) levels below 1 mg/dL, in contrast to neonates, where TSB levels are physiologically high. Healthy full-term neonates also have an increased bilirubin load due to increased red blood cell (RBC) mass and shortened RBC lifespan. Bilirubin clearance is also affected by impaired activity of uridine diphosphate glucuronosyltransferase (UGT), an enzyme required for bilirubin conjugation. UGT enzymes have activity in neonates that is approximately 1% of adult levels. In addition, these infants also have increased enterohepatic circulation, further contributing to elevated TSB levels. Physiological jaundice usually develops 24 hours after birth, peaks at approximately 48–96 hours, and in term infants he resolves in 2–3 weeks (Lawrence, 2002).

Human breast milk factors that may be associated with the etiology of breast milk jaundice include pregnane-3α, 20β-diol, interleukin IL1β, β-glucuronidase, epidermal growth factor, and α-fetoprotein (Stephanie et al. 2021). The presence of pregnane-3α,20β-diol is thought to inhibit bilirubin conjugation and prevent bilirubin excretion. β-glucuronidase is an endogenous enzyme that deconjugates bilirubin at the intestinal brush border, resulting in increased serum reabsorption rather than excretion (Preer et al., 2011). Studies have shown that the activity of this enzyme is negligible in infant formula but significant in breast milk (el-Kholy et al., 1992). The cholestatic effect has been attributed to interleukin Iβ, which causes hyperbilirubinemia (Stephanie et al., 2021). Epidermal growth factor is present at high levels in human breast milk and in the serum of strictly breastfed infants. This is because it enhances intestinal absorption of bilirubin, reduces

intestinal motility in the neonatal period, and increases levels of unconjugated bilirubin (Preer et al., 2011). Serum from babies with breast-fed jaundice often shows elevated alpha-fetoprotein levels. The underlying mechanism is still unknown

Jaundice is considered pathological if it presents on the first day of life, TSB is more than the 95th centile for age based on age-specific bilirubin monograms, levels rise by more than 5 mg/dl/day or more than 0.2 mg/dl/hour, or jaundice persists beyond 2 to 3 weeks in full-term infants.

Based on the mechanism of bilirubin elevation, the etiology of unconjugated hyperbilirubinemia can be subdivided into the following three categories:

1. **Increased Bilirubin Production**

- Immune-mediated hemolysis: Includes blood group incompatibilities such as ABO and Rhesus incompatibility.
- Non-immune mediated hemolysis: includes RBC membrane defects like hereditary spherocytosis and elliptocytosis; RBC enzyme defects like glucose-6-phosphate dehydrogenase (G6PD) deficiency; pyruvate kinase deficiency; sequestration like cephalohematoma, subgaleal hemorrhage, intracranial hemorrhage; polycythemia, and sepsis.

2. **Decreased Bilirubin Clearance**

   Crigler-Najjar type I & II, and Gilbert syndrome

3. **Miscellaneous Causes**

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Other causes include maternal and child diabetes, congenital hypothyroidism, medications such as sulfa drugs, ceftriaxone, and penicillin, intestinal obstruction, pyloric stenosis, breastfeeding jaundice, and breastfeeding jaundice.

Rhesus (Rh) incompatibility sensitizes Rh-negative mothers who have been exposed to Rh-positive red blood cells, usually from a previous pregnancy or miscarriage, to develop antibodies to Rh antigens. Sensitization initially produces her IgM antibodies that cannot cross the placenta. However, during subsequent pregnancies, antibody class switching generates IgG antibodies that cross the placenta and cause erythrocyte hemolysis in fetuses with Rh-positive blood. The Rh antigen is highly immunogenic and the resulting hemolytic disease of the newborn (HDN) is usually severe and often causes fetal edema (Lawrence, 2002). Indirect hyperbilirubinemia due to decreased bilirubin clearance usually results from quantitative or qualitative defects in the enzyme uridine diphosphate glucuronosyltransferase (UGT). Gilbert syndrome, Crigler-Najjar syndrome type 1, and Crigler-Najjar syndrome type 2 are three classic disorders caused by abnormalities in UGT enzymes. Gilbert's syndrome is the most common of these, where mutations in the UGT1A1 gene lead to decreased UGT production and unconjugated hyperbilirubinemia. Gilbert's syndrome usually presents as mild jaundice during stress without hemolysis or liver dysfunction. Neonatal onset is rare and usually he is associated with G6PD. Crigler-Najjar syndrome type 1 is an AR disorder resulting from a complete lack of UGT activity. Affected patients present with severe hyperbilirubinemia in the first few days of life, often leading to bilirubin encephalopathy. Patients with Crigler-Najjar syndrome type 2 retain some activity of UGT enzymes. Therefore, TSB levels are not very high and patients rarely develop bilirubin encephalopathy (Betty et al., 2022).

Breastfeeding jaundice and lactation jaundice are two other common causes of UHB in newborns. Breastfeeding jaundice, also known as breastfeeding failure jaundice, occurs in the first week of life and can be caused by insufficient breast milk intake, leading to dehydration and hypernatremia. Failure to breastfeed results in decreased intestinal motility and decreased excretion of bilirubin in the stool or meconium. Breast milk jaundice appears in the first week of life, peaks in the second

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week, and usually resolves by the time she is two weeks old. This is mainly attributed to inhibition of UGT enzymes by pregnanediol and deconjugation of intestinal conjugated bilirubin by beta-glucuronidase in breast milk (Peer et al., 2011). Various other causes of UHB include infants born to diabetic mothers (IDM), gastrointestinal obstruction, congenital hypothyroidism, and certain medications. IDMs often suffer from polycythemia, which is primarily responsible for the increased incidence of jaundice in these infants. His UHB in congenital hypothyroidism is associated with decreased hepatic bilirubin uptake, impaired UGT activity, and decreased intestinal motility. Gastrointestinal obstruction promotes increased recycling of bilirubin by increasing enterohepatic circulation. When used in the neonatal period, certain drugs may exacerbate her UHB by displacing bilirubin from albumin and interfering with albumin binding. Sepsis may also predispose neonates to UHB by causing oxidative damage to red blood cells and increasing bilirubin load (Rubath et al., 2013).

Type 2 Conjugated Hyperbilirubinemia (CHB) or Direct Hyperbilirubinemia

Conjugated hyperbilirubinemia, also referred to as neonatal cholestasis, is characterized by elevation of serum conjugated/direct) bilirubin (> 1.0 mg/dl) and is due to impaired hepatobiliary function. Distinguishing CHB from UHB is critical because cholestatic jaundice/CHB is almost always pathologic and warrants prompt evaluation and treatment (Fawaz *et al*., 2017).

The causes of neonatal cholestasis/CHB are extensive and can be classified into the following categories:

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.

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3. **Genetic causes**: Alagille syndrome, alpha-1 anti-trypsin deficiency, galactosemia, fructosemia, Tyrosinemia type 1, cystic fibrosis, progressive familial intrahepatic cholestasis (PFIC), Aegean's syndrome, Dubbin-Johnson syndrome, Bile acid synthesis disorders(BSAD).

4. **Miscellaneous:** Idiopathic neonatal hepatitis, parenteral nutrition induced cholestasis, gestational alloimmune liver disease/neonatal hemochromatosis, hypotension.

Biliary atresia (BA) is the most common cause of conjugated hyperbilirubinemia in infants. The incidence of BA varies by region. Taiwan, the region with the highest incidence, reports a birth rate of 1 in 6000 live births. It occurs in approximately 1 in 12,000 live births in the United States. The etiology of BA is poorly understood, but genetic factors appear to play a role in its pathogenesis, along with viral infections, toxins, chronic inflammation, and autoimmune damage to the bile ducts. The disease affects both intrahepatic and extrahepatic bile ducts and typically presents with pale stools and jaundice around 2 to 4 weeks of age. The initial evaluation is by ultrasound, which may show the absence of a gallbladder and the classic "trigonoid" signs. Early diagnosis is critical for maximizing response to Kasai (hepatic portal vein incision) surgery. If surgery is delayed by 90 days after birth, less than 25% of patients will respond, but if more than 70% of patients establish adequate bile flow, surgery will be performed within 60 days (Betty et al., 2022).

Parenteral nutrition-associated cholestasis (PNAC) is an important iatrogenic cause of cholestasis, most commonly recognized in preterm infants treated with parenteral nutrition (PN). PNAC is present in approximately 20% of neonates who have had PN for 2 weeks or longer. Duration of PN use and intestinal failure are her two independent risk factors for PNAC. Its mechanism is not entirely clear and is probably multifactorial. The main causes are thought to be the abnormal metabolism of bile salts by premature infants and the adverse effects of PN components. Other factors, such as sepsis and necrotizing enterocolitis, appear to enhance liver damage. Alloimmune Obeagu, E.I and Katya, M.C. (2022). A SYSTEMATIC REVIEW ON PHYSIOLOGICAL JAUNDICE: DIAGNOSIS AND MANAGEMENT OF THE AFFECTED NEONATES. Madonna University Journal of Medicine and Health Science. 2 (3):25-41

gestational liver disease (GALD) is a fulminant alloimmune disease that causes almost all cases of neonatal hemochromatosis and results from intrahepatic and extrahepatic iron deposition leading to liver failure (Betty et al., 2022).

In GALD, maternal her IgG immunoglobulin against fetal liver cells crosses the placenta and causes complement-mediated damage to fetal liver cells. Patients present with signs of liver failure in the form of hypoglycemia, coagulopathy, hypoalbuminemia, cholestatic jaundice, edema, and increased liver enzymes. With nearly a 90% risk of recurrence in subsequent pregnancies, GALD can lead to fetal or neonatal death. The term idiopathic neonatal hepatitis is used when the etiology of neonatal cholestasis cannot be clarified after extensive diagnostic workup. The size of this entity will shrink accordingly

FACTORS INFLUENCING PHYSIOLOGICAL OR NEONATAL JAUNDICE

Maternal risk factors

Table 1. Maternal risk factors

Aspect	Comment
Blood group	• Blood group O • Rhesus D (RhD) negative • Red cell antibodies—D,C,c,E,e and K and certain others[24]
Previous jaundiced baby[23]	• Required phototherapy or other treatment
Diabetes[23]	• High red cell mass in baby where maternal diabetes is poorly controlled diabetes (any type).
Genetic	• East Asian[23] • Mediterranean[14] • Family history of inherited haemolytic disorders (e.g. G6PD deficiency, hereditary spherocytosis)[23]

Neonatal risk factors

Table 2. Neonatal risk factors

Aspect	Comment
Feeding	• Breast milk: ○ β glucuronidase in breast milk increases the breakdown of conjugated bilirubin to unconjugated bilirubin in the gut[4] ○ Lipoprotein lipase (a water-soluble enzyme) and nonesterified fatty acids in breast milk may inhibit normal bilirubin metabolism[25,26] • Factors that delay normal colonisation with gut bacteria resulting in high concentration of bilirubin in the gut) • Low breast milk (may be due to delayed milk production) or formula intake leading to dehydration and increased enterohepatic circulation[4,27]
Haematological[18,23,28]	• Factors causing haemolysis (immune or non-immune)[4] • Polycythaemia • Haematoma or bruising
Gastrointestinal[29]	• Bowel obstruction
Other[4,23]	• Infection • Prematurity • Male

(Queensland Government, 2019)

DIAGNOSIS

Clinical assessment of jaundice

- The parents should be counselled regarding benign nature of jaundice in most neonates, and for the need to be watchful and seek help if baby appears too yellow. The parents should be explained about how to see for jaundice in babies (in natural light, no yellow background and see skin and eyes of the baby).
- Visual inspection of jaundice (Panel) is believed to be unreliable, but if it is performed properly (i.e., examining a naked baby in bright natural light and in absence of yellow background), it has reasonable accuracy (as good as transcutaneous bilirubinometry if done diligently) particularly when TSB is less than 12 to 14 mg/dL or so. Absence of jaundice on visual inspection reliably excludes the jaundice. At higher TSBs, visual inspection is unreliable and, therefore, TSB should be measured to ascertain the level of jaundice.

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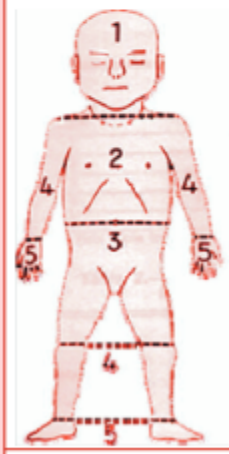
- All neonates should be examined at every opportunity but not lesser than every 12 hr during first 3 to 5 days of life for jaundice. The babies being discharged from the hospital at 48 to 72 hours should be seen again after 48 to 72 hours of discharge (TSB peaks at around 72 hours in term babies and later than 72 hours in preterm babies).
- The neonates at higher risk of jaundice should be identified at birth and kept under enhanced surveillance for occurrence and progression of jaundice (see risk factors) (*Section 5 Gastrointestinal and Hepatobiliary*, n.d.).

Panel 1 Visual inspection of jaundice

1. Examine the baby in bright natural light. Alternatively, the baby can be examined in bright white fluorescent light. Make sure there is no yellow or off-white background. You may have to move the baby from mother's bed/OPD to a brightly lit area.
2. The baby should be naked.
3. Examine blanched skin and gums or sclerae
4. Note the extent of jaundice (Kramer's rule)[6]
5. *Depth of jaundice (degree of yellowness) should be carefully noted (light staining as lemon yellow; deep staining as orange yellow),* as it is an important indicator of level of jaundice and it does not figure out in Kramer's rule.
   A deep yellow staining (even in absence of yellow soles or palms) may be associated with severe jaundice and therefore TSB should be estimated in such circumstances.



Kramer zones	Approximate TSB level	
	Mild jaundice (Lemon yellow color)	Deep jaundice (Orange yellow color)
1 (Face and neck)	5 to 7 mg/dL	7 to 9 mg/dL
2 (Chest and upper abdomen)	7 to 9 mg/dL	9 to 11 mg/dL
3 (Lower abdomen and thighs)	9 to 11 mg/dL	11 to 13 mg/dL
4 (Legs and arms/ forearms)	11 to 13 mg/dL	14 to 16 mg/dL
5 (Palms and soles)	13 to 15 mg/dL	17 mg/dL or more

Investigations

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1. **Initial evaluation**:

   • Total and direct bilirubin

   • Blood type and Rh (infant & mother)
   • Hematocrit
   • Direct Antiglobulin (Coombs) Test on infant

2. **Later evaluation (as indicated):**

   • RBC smear, reticulocyte count (if evidence or suspicion of hemolytic disease)
   • Blood culture, urinalysis, urine culture
   • Thyroid function tests, G6PD assay, Hgb electrophoresis

All babies should have their total bilirubin measured before discharge from the maternity hospital. Compared to selective testing, universal screening reduces the total blood draw and phototherapy rate. Several clinical risk scores have been developed, but none are as predictive of later hyperbilirubinemia as predischarge bilirubin levels.

Transcutaneous (TcB) levels should be used for screening. Transcutaneous levels are reasonable estimates of serum levels and can be performed quickly without blood sampling. TcB should be obtained from the neonatal sternum to avoid false-negative results that may be related to exposure of the neonate's face to the sun.

Pre-discharge bilirubin levels should be used as a guide for follow-up. Significant hyperbilirubinemia in this case is defined as above the 95th percentile on the nomogram and does

not necessarily correlate with the need for phototherapy or exchange transfusion, length of hospital stay, or neurological outcome. Hourly nomograms have been validated for ABO ineligible and direct antiglobulin test-positive patients and can be used in this population.

Serum bilirubin (TSB) is recommended in the situations described in Table 3. Tests recommended when investigating the underlying etiology of indirect hyperbilirubinemia include DAT, if not already done, G6PD, hemoglobin/hematocrit, reticulocyte count, and peripheral blood smear (RBC index).), differential complete blood count, blood culture, and urine culture.

Table 3. Indications for Bilirubin Testing Modalities and Infant Jaundice Studies

Trans-cutaneous Bilirubin (TcB)	Total Serum Bilirubin(TSB)	Infant Jaundice Study (IJS)
Reasonable estimate for serum bilirubin levels when the level is < 13mg/dL. • TcB should be obtained from the sternum. • TcB may be used for trending, when there is clinical suspicion of hyperbilirubinemia. In the outpatient setting (clinic or visiting nurses), TcB may be used to assess neonatal hyperbilirubinemia.	The **initial** serum bilirubin should be fractionated to evaluate for direct hyperbilirubinemia. Subsequent draws can be total bilirubin alone. Obtain when: Considering phototherapy or other treatment *[I-C]* Management would change at TcB +3 TcB is >15 *[I-C]*[3] There is visible jaundice in the first 24 hours *[II-D]*[4]	**Obtain when:** Considering phototherapy or other treatment. *[I-D]** Mother has not had prenatal testing for blood type and antibody screen. *[I-D]* Mother has potentially significant antibodies *[I-D]* Bilirubin is less than treatment threshold, but rapidly rising (rate of rise > 0.2mg/dL/hr). *[II-D]*
Contraindications: Do not use TcB if phototherapy has been initiated Do not use TcB situations where rapid rise in serum values are anticipated (eg, active hemolysis). TcB can underestimate serum values in these situations		**Not routinely obtained:** All mothers with blood type O. Use only when indicated (see above). All Rh+ neonates of Rh- mothers who were treated with Rho(D) immune globulin (e.g. rophylac, RhoGAM™). DAT has a low positive predictive value for later hyperbilirubinemia and there is a risk of false positive after RhoGAM. Use only when indicated (see above).

DAT = *direct antiglobulin test*

*May consider sending IJS when TcB is within 3 mg/dL of 'neurotoxicity risk factor present' treatment threshold

(Sroufe and Vredeveld, 2020)

COMPLICATIONS

Newborns with severe hyperbilirubinemia are at risk for bilirubin-induced neurological dysfunction (BIND). Bilirubin binds to the globus pallidus, hippocampus, cerebellum, and subthalamic nucleolus, causing neurotoxicity. Acutely, it presents as acute bilirubin encephalopathy (ABE), characterized by lethargy, hypotension, and decreased sucking. At this stage, the disease is reversible. However, as ABE progresses, patients may develop chronic bilirubinic encephalopathy/kernicterus, which is irreversible. It manifests as choreiform cerebral

palsy, seizures, arching, postural, gaze abnormalities, and sensorineural hearing loss. Patients with neonatal cholestasis are at risk of developing liver failure, cirrhosis, and possibly hepatocellular carcinoma. Prolonged cholestasis can also lead to impaired growth and deficiencies of fat-soluble vitamins (Betty, 2022).

PREVENTION

The best preventive of infant jaundice is adequate feeding. Breast-fed infants should have eight to 12 feedings a day for the first several days of life. Formula-fed infants usually should have 1 to 2 ounces (about 30 to 60 milliliters) of formula every two to three hours for the first week (Sroufe and Vredeveld, 2020).

TRAITEMENT OF PHYSIOLOGICAL JAUNDICE

1. Treatment of Unconjugated Hyperbilirubinemia

Phototherapy and exchange transfusion are the mainstay of treatment for patients with unconjugated hyperbilirubinemia.

2. Phototherapy

Phototherapy (PT) remains the first-line treatment for managing pathological unconjugated hyperbilirubinemia. PT is very effective in reducing TSB to safe levels and reduces the risk of bilirubin toxicity and the need for exchange transfusion. Phototherapy is started based on risk factors and the TSB levels on the bilirubin nomogram. The efficacy of phototherapy depends on the dose and wavelength of light used as well as the surface area of the infant's body exposed to it. Increasing the dose of PT can be achieved by placing phototherapy units at the minimum safe distance from the infant and increasing the number of units used (Betty, 2022).

3. Exchange Transfusion

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4. Exchange transfusion (ET) was the first successful treatment ever used for jaundice and is now the second-line treatment for severe unconjugated hyperbilirubinemia. Appears when the PT is unresponsive or the initial TSB level is within the exchange range based on the nomogram. ET rapidly clears bilirubin and hemolysis. Hemolysis causes antibodies to leak out of the circulation. A double volume exchange (160-180 ml/kg) transfusion is performed to replace the neonatal blood with split crossover blood. Because the majority of systemic bilirubin resides in complications of the extravascular compartment, TSB levels are approximately 60% of preexchange levels immediately after ET and rise to 70–80% of preexchange levels afterward. Equilibrium with the extravascular increased portion of bilirubin. Vital signs should be closely monitored during ET, and TSB, CBC, serum calcium, glucose, and electrolytes should be checked after the procedure. Complications of ET include electrolyte abnormalities such as hypocalcemia and hyperkalemia, cardiac arrhythmias, thrombocytopenia, blood infections, portal vein thrombosis, graft-versus-host disease, and necrotizing enterocolitis (NEC). included. Phototherapy should be continued after exchange transfusion until bilirubin levels reach levels that can be safely discontinued (Jackson, 1997).

5. **Intravenous Immunoglobulin (IVIG)**

IVIG is used when immune-mediated hemolysis is the cause of UHB jaundice and prevents RBC hemolysis by coating Fc receptors on RBCs. The AAP recommends IVIG infusion in immune-mediated hemolysis if TSB remains within 2 to 3 mg/dl of exchange level despite intensive phototherapy. However, the evidence that the use of IVIG reduces the need for ET is not very clear. Nonetheless, IVIG is often used in clinical practice to manage unconjugated hyperbilirubinemia (Alpay *et al*., 1999).

6. **Treatment of Conjugated Hyperbilirubinemia**

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Treatment of conjugated hyperbilirubinemia is tailored to the specific etiology. Patients diagnosed with biliary atresia require Kasai (hepatoportoenterostomy) surgery, preferably within the first two months of life for best results. Kasai surgery involves removal of the obstructed bile duct and fibrous lamina, and Rouen Y anastomosis of the jejunum with the remaining duct to provide an alternative route for biliary drainage. Infectious causes of cholestasis are treated with specific antibiotics, but treatment with cholic acid and chenodeoxycholic acid is often curative in many BASDs. Addresses sexually transmitted diseases and improves liver function. GALD patients seem to respond well to IVIG and double exchange transfusions. Liver transplantation, when available, is curative but technically challenging in this age group (Chukwurah et al., 2019). Cholestasis induced by parenteral nutrition is treated with cyclic PN, exposure duration is shortened, and enteral nutrition is started as soon as possible. To minimize liver damage, the manganese and copper content of PN should be reduced (Ohi, 2001).

CONCLUSION AND RECOMANDATION

Neonatal jaundice is relatively common and characterized by hyperbilirubinemia. However, babies diagnosed with both unconjugated jaundice (mostly) and conjugated jaundice should be evaluated and treated in collaboration with a physician who has liver experience. This should be noted. Many conditions that cause jaundice are not readily diagnosed, but education about the condition is very important. Nurses and parents are often the first to notice jaundice in newborns. After discharge from the maternity hospital, parents should be educated by nurses, pediatricians, obstetricians, and family physicians' offices to watch for jaundice and seek medical attention if it worsens.

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