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A NARRATIVE REVIEW ON NEONATAL JAUNDICE

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ABSTRACT

Neonatal jaundice is a prevalent condition characterized by yellow discoloration of the skin, sclera, and mucous membranes due to elevated total serum bilirubin (TSB) levels. Affecting approximately 60% of full-term and 80% of preterm infants, neonatal jaundice is typically benign but can lead to severe complications if not managed appropriately. Prolonged jaundice can result in kernicterus and bilirubin encephalopathy, necessitating prompt medical intervention. The aim was to provide a brief review on the etiology, epidemiology, clinical manifestations, risk factors, diagnostic methods and management strategies of neonatal jaundice. Unconjugated hyperbilirubinemia is most often physiological but can also be pathological due to factors such as hemolysis (e.g., ABO/Rh incompatibility, G6PD deficiency) or genetic disorders (e.g., Gilbert syndrome). Conjugated hyperbilirubinemia, less common but always pathological, is primarily caused by hepatobiliary dysfunctions such as biliary atresia or genetic syndromes. Clinical manifestations range from mild yellowing of the skin to severe symptoms like lethargy and high-pitched crying. Early diagnosis through physical examination, bilirubin level measurement, and risk assessment is critical. Treatment strategies include enhanced nutrition, phototherapy, exchange transfusion and intravenous immunoglobulin (IVIg), depending on the severity and underlying cause. Phototherapy remains the mainstay for treating hyperbilirubinemia, while exchange transfusion and IVIg are reserved for severe cases, particularly those involving immune-mediated hemolysis. While neonatal jaundice is common and usually benign, early detection and appropriate

management are vital to prevent severe complications. Continued research and education are essential to optimize outcomes for affected infants.

KEYWORDS: Neonatal jaundice, hyperbilirubinemia, bilirubin, phototherapy, exchange transfusion.

INTRODUCTION

Neonatal jaundice is clinically characterized by a yellowish coloration of the skin, sclera and mucous membranes and is caused by a high total serum bilirubin (TSB) level.[2] Neonatal jaundice is one of the most common conditions requiring medical attention.[1] Increased red cell breakdown and reduced bilirubin excretion cause the majority of jaundice in newborns.[3] The French word "jaune," which implies yellow, is where the word "jaundice" originates.[2]

Neonatal jaundice is quite common, affecting about 60% of full-term babies and 80% of premature babies.[1] Premature babies and male infants are at a higher risk of developing jaundice[4], around 10% of breastfed infants have a chance of getting jaundiced at one month, and 60% of infants, and 80% of premature babies develop jaundice within 2 to 4 days after birth and goes away on its own in 1 to 2 weeks.[5]

Prolonged jaundice, lasting beyond 14 days, can have severe consequences and requires prompt medical attention.[6] Newborns with darker skin may present with clinically significant jaundice that may not be apparent on visual inspection, despite elevated bilirubin levels. The yellowing of the hands and soles of the feet, a common sign of jaundice, typically appears within the first 24 hours after birth and resolves by the end of the first week.[7] Genetic polymorphisms and race are among the key factors that can cause elevated bilirubin levels.[4]

Infantile jaundice has an incidence rate of approximately 1 in 2500 to 5000 live births. This condition can be attributed to various underlying diagnoses, ranging from less severe cases like breast milk jaundice, to more critical conditions such as biliary atresia or liver failure.[8]

Close monitoring of bilirubin levels is crucial in the management of neonatal jaundice. Although unconjugated bilirubin levels beyond a particular threshold may infrequently cause irreversible brain damage, kernicterus is one of them. Failure to recognize and manage neonatal jaundice could lead to bilirubin encephalopathy and neurological consequences.[9]

Jaundice in the newborn has a reported incidence between 60% to 90% and global incidence of 99/100,000 or higher, affecting 130,000 or more newborns per year. Severe jaundice accounted for 15.3% of neonatal admissions in India, with a CFR of 6.7% and 4.4% of jaundice-related deaths. China has 49.1%, Myanmar has 46%, Malaysia has 25-30%, and Indonesia has 6.8% of serous jaundice and 1.6% of death linked jaundice.[10][11][12][13][14][15]

A family history of neonatal jaundice increases the risk of jaundice in the newborn. It is one of the genetic disorders that lead to endocrine and metabolic conditions and maternal diabetes. Medication taken by the mother during pregnancy can affect the newborn's hepatic bilirubin metabolism. Birth trauma causes jaundice with excess bilirubin production due to blood extravasation. Preterm newborns have an underdeveloped bilirubin metabolism and are more prone to jaundice. Breast-fed newborns are more likely to develop jaundice.[10][16]

It's important to remember that neonatal jaundice is a common and usually harmless condition. However, if you notice any concerning signs or symptoms, such as a baby being lethargic, having difficulty feeding, or having a high-pitched cry, it's important to seek medical attention promptly.

Etiology

There are two types of neonatal hyperbilirubinemia.

1. Unconjugated Hyperbilirubinemia (UHB) or Indirect Hyperbilirubinemia

Unconjugated hyperbilirubinemia is the most common form of jaundice, which can be either normal or pathological.[11] Physiological jaundice accounts for 75% of newborn hyperbilirubinemia and is caused by a change in neonatal bilirubin metabolism.[12] Bilirubin clearance is hindered by decreased activity of uridine diphosphate glucuronosyltransferase (UGT); the enzyme required for bilirubin conjugation.[13] Furthermore, newborns have enhanced enterohepatic circulation, which contributes to elevated TSB levels. In full-term infants, physiological jaundice typically begins at 24 hours of age, peaks around 48-96 hours, and resolves in two to three weeks.[14] Pathological jaundice occurs when TSB exceeds the 95th centile for age based on age-specific bilirubin nomograms, levels rise by more than 5 mg/dL/day or more than 0.2 mg/dL/hour, or jaundice lasts more than 2 to 3 weeks in full-term newborns.[15]

The etiology of unconjugated hyperbilirubinemia can be categorized into three types based on the mechanism of bilirubin increase.[16]

Increased Bilirubin Production

Hemolysis can be caused by immune-mediated and non-immune-mediated factors. Immune-mediated hemolysis can result from blood group incompatibilities such as ABO and Rhesus.[17] Non-immune-mediated hemolysis can be caused by various factors such as RBC membrane defects like hereditary spherocytosis and elliptocytosis, RBC enzyme defects like glucose-6-phosphate dehydrogenase (G6PD) deficiency, and pyruvate kinase deficiency, sequestration like cephalohematoma, subgaleal hemorrhage, and intracranial hemorrhage, polycythemia, and sepsis.[18][19]

Decreased Bilirubin Clearance

Crigler-Najjar types I and II, as well as Gilbert syndrome.[20]

Miscellaneous Causes

Pathological hyperbilirubinemia in infants can be caused by various factors such as congenital hypothyroidism, medicines like sulfa pharmaceuticals, ceftriaxone, and penicillins, intestinal obstruction, pyloric stenosis, breast milk jaundice, and breastfeeding jaundice.[21] The most common cause of pathological hyperbilirubinemia in infants is exaggerated hemolysis, which can be immune or non-immune caused.[22] Immune-mediated hemolysis occurs due to blood type incompatibilities, such as ABO/RH incompatibility, and results in hemolytic disease of neonates (HDN).[23] In HDN due to ABO incompatibility, performed maternal anti-A and anti-B antibodies of the immunoglobulin (Ig) G subclass cause hemolysis and UHB in babies with blood types A, B, or AB. Rh incompatibility occurs when a Rh-negative mother who has been exposed to Rh-positive RBCs during a prior pregnancy or miscarriage gets sensitized and produces antibodies against the Rh antigen.[24][25]

Hereditary spherocytosis (HS) and hereditary elliptocytosis (HE) are types of UHB caused by RBC membrane abnormalities.[26] HS is the most frequent RBC membrane defect caused by mutations in RBC membrane proteins and is transmitted as an autosomal dominant (AD) characteristic.[27] Hereditary elliptocytosis is another RBC membrane abnormality that is typically asymptomatic but can cause UHB in newborns. Subgaleal haemorrhages, intracranial haemorrhages, and RBC sequestrations from cephalohematomas are all causes or risk factors for UHB in the neonatal era.

Polycythaemia is another condition linked to an increased risk of UHB in newborns and is associated with factors such as intrauterine growth restriction (IUGR), infant of diabetic mothers (IDM), big for gestational age (LGA), maternal smoking, high altitude, twin to twin transfusion, and placental transfusion (delayed cord clamping/umbilical cord milking).[28][29]

2. Conjugated Hyperbilirubinemia (CHB) or Direct Hyperbilirubinemia

Conjugated hyperbilirubinemia, also referred to as newborn cholestasis, is a medical condition characterized by an increase in serum conjugated/direct bilirubin (> 1.0 mg/dL) caused by poor hepatobiliary function. It is crucial to differentiate CHB from UHB as cholestatic jaundice/CHB is almost always pathologic and requires immediate investigation and treatment.[30]

The causes of newborn cholestasis/CHB are numerous and can be categorized as follows.

- **Biliary obstructions flow** includes choledochal cysts biliary atresia, and neonatal cholelithiasis, and neonatal sclerosing cholangitis.
- **Infections**: HIV, urinary tract infection (UTI), rubella, septicemia, herpes virus, syphilis, CMV, toxoplasmosis.
- **Genetic causes:** Alagille syndrome, Aagenaes syndrome, galactosemia, fructosemia, cystic fibrosis, Dubin-Johnson syndrome, progressive familial intrahepatic cholestasis (PFIC), alpha-1 anti-trypsin deficiency, Tyrosinemia type 1, Bile acid synthesis disorders (BSAD).
- **Miscellaneous:** The most prevalent cause of conjugated hyperbilirubinemia in babies is biliary atresia (BA). gestational alloimmune, liver disease, Idiopathic neonatal hepatitis, hypotension parenteral nutrition-induced cholestasis neonatal hemochromatosis.[31]

CLINICAL MANIFESTATION

It is imperative to recognize the symptoms of jaundice in infants. One of the characteristic signs is a mild yellowing of the skin, which may be more prominent in particular regions such as the sclera, mouth, soles of the feet, and palms of the hands.[31][32]

In infants with darker skin, the alteration in skin color may be more challenging to discern. Furthermore, the skin on the head and face may demonstrate more noticeable jaundice.[33]

1. Yellowing of the skin and eyes: The most noticeable sign of neonatal jaundice is the yellow discoloration of the baby's skin and the whites of their eyes. This yellowing usually starts on the face and then spreads to the chest, abdomen, and limbs.

2. Changes in stool and urine color: Babies with jaundice may have pale or clay-coloured stools and dark yellow urine. This is because bilirubin is excreted through the stool and urine.

3. Poor feeding and lethargy: Some babies with jaundice may show signs of being sleepy, lethargic, or have difficulty waking up for feedings. They may also have a weak suck and may not feed as vigorously as usual.

4. High-pitched cry: In rare cases, babies with severe jaundice may have a high-pitched cry that sounds different from their usual cry. This can be a sign of more severe jaundice and requires immediate medical attention.

5. Changes in muscle tone: Jaundiced babies may appear floppy or have decreased muscle tone. They may seem less active or have a weak grasp reflex.

6. Other symptoms: include excessive sleepiness, poor feeding, dry diapers, a high-pitched cry, strange or abnormal eye movements, and yellowing of the face, scalp, and body.[34]

It's important to note that mild jaundice is quite common in newborns and usually resolves on its own without any treatment. It is essential for parents and caregivers to be aware of these symptoms and to seek medical attention if they suspect jaundice in their infant. However, if you notice any of these signs or if the jaundice appears to be worsening, it's important to seek medical advice. Healthcare providers can perform a physical examination and conduct tests to determine the severity of the jaundice and the appropriate course of action.[35][36]

Epidemiology

Unconjugated hyperbilirubinemia is a common condition in newborns, with a reported incidence of 60% in term and 80% in preterm infants, characterized by clinical jaundice and total serum bilirubin (TSB) levels above 5 mg/dl.[37] However, only a minority of neonates require phototherapy for jaundice.[38] Physiological jaundice is the most common cause of clinical jaundice after the first day of life, accounting for almost half of all cases.[39] Approximately 15% of breastfed newborns will develop unconjugated hyperbilirubinemia that persists beyond three weeks.[40] Only a small proportion of neonatal jaundice cases are due to pathological causes, with severe hyperbilirubinemia affecting around 1 in every 2500 live births.[41] ABO incompatibility is the most commonly identified cause, followed by G6PD deficiency. Neonatal jaundice appears to be more prevalent in individuals who reside

at high altitudes and near the Mediterranean Sea, particularly in Greece.[42][43] The incidence of acute bilirubin encephalopathy is approximately one in every 10,000 live births, but the incidence of chronic bilirubin encephalopathy is estimated to be one in every 50,000 to 100,000 live births.[44][45] However, the incidence of kernicterus is significantly higher in developing countries.[46] Conjugated hyperbilirubinemia is much less frequent than unconjugated hyperbilirubinemia and is almost always pathological.[47][48][49]

Pathophysiology

Bilirubin is produced in the reticuloendothelial system (RES) by the catabolism of heme, a breakdown product of haemoglobin.[50] The enzyme heme oxygenase converts heme to biliverdin, releasing iron and carbon monoxide. Biliverdin reductase then converts biliverdin to bilirubin. This unconjugated bilirubin is hydrophobic and is transported to the liver attached to albumin, where it is conjugated with glucuronic acid by the enzyme uridine diphosphate-glucuronosyltransferase (UGT) in the smooth endoplasmic reticulum. After being metabolized by intestinal bacterial flora, conjugated bilirubin is expelled in bile and the gastrointestinal (GI) tract, where it is primarily eliminated in feces. Some conjugated bilirubin is deconjugated in the GI tract by beta-glucuronidase and reabsorbed via enterohepatic circulation.[51][52]

Newborns have higher haemoglobin levels at birth, a shorter red blood cell life span, and a reduced conjugating ability of the newborn liver, which leads to higher total serum bilirubin levels than adults. As a result, full-term babies typically have peak blood bilirubin concentrations of 5 to 6 mg/dl, whereas adults have levels of 1 mg/dl.[54] Pathological jaundice in newborns is associated with increased bilirubin synthesis in RES, decreased hepatic absorption, bilirubin conjugation deficiencies, and/or increased enterohepatic bilirubin circulation. Unbound and unconjugated bilirubin crosses the blood-brain barrier and binds to the brainstem, hippocampus, and basal ganglia, which can lead to bilirubin-induced neurologic dysfunction (BIND) and acute bilirubin encephalopathy (ABE). Infants with ABE can exhibit lethargy, poor feeding, high-pitched crying, hypertonia, and seizures.[55] Treatment for neonatal jaundice usually involves phototherapy to convert unconjugated bilirubin to a water-soluble form that can be excreted in the urine, or in severe cases, exchange transfusion to replace the infant's blood with donor blood. Phototherapy is effective for most infants with unconjugated hyperbilirubinemia, but in rare cases, severe hyperbilirubinemia can cause kernicterus.[56]

Conjugated hyperbilirubinemia is a condition that can be caused by various anomalies in the metabolism, transport, uptake, and excretion of bile salts and bilirubin. These anomalies can lead to an increase in bile acid in the liver, which can cause fibrosis and growth of bile ducts, inflammation, and apoptosis of hepatocytes.[57] Cholestasis, which is characterized by insufficient bile secretion, can also cause malabsorption of fat and fat-soluble vitamins, leading to deficiencies in vitamins A, D, E, and K and failure to thrive.[58]

Types of Neonatal Jaundice

1. Physiological Jaundice: This is the most common type of neonatal jaundice, affecting over half of all newborns. It typically appears after the first day of birth and peaks around the third to fifth day. Physiological jaundice occurs due to the immaturity of the baby's liver, which may take a few days to efficiently process bilirubin. It usually disappears by itself within two weeks.

2. Breastfeeding Jaundice: Breastfeeding jaundice can occur when a baby is not getting enough breast milk. Inadequate intake can lead to dehydration, which concentrates the bilirubin in the blood. This type of jaundice typically appears within the first week of life and can be resolved by ensuring proper breastfeeding techniques and frequent feeding.

3. Breast Milk Jaundice: Breast milk jaundice is a less common type that occurs when certain substances in breast milk interfere with the breakdown of bilirubin in the baby's liver. It usually occurs after the first week of life and can last for several weeks. Most cases of breast milk jaundice resolve on their own without any complications.

4. Hemolytic Jaundice: Hemolytic jaundice occurs when there is an increased breakdown of red blood cells, leading to higher levels of bilirubin. This can be caused by blood group incompatibility between the mother and baby, such as Rh or ABO incompatibility. Hemolytic jaundice may require medical intervention to manage the underlying cause and prevent complications.

5. Infection-related Jaundice: Certain infections, such as urinary tract infections or sepsis, can cause neonatal jaundice. In these cases, the infection affects the liver's ability to process bilirubin, leading to elevated levels. Prompt diagnosis and treatment of the underlying infection are crucial to prevent complications.

6. Early neonatal jaundice is common but usually harmless. It resolves on its own within a couple of weeks occurs within 24 hours.[59][60][61][62]

RISK FACTORS[63][64][65]

1. Premature birth: Babies born before the 37th week of pregnancy are at a higher risk of jaundice as their liver may not yet be fully developed.

2. Blood type incompatibility: If a baby's blood type is different from their mother's, it can lead to an increased risk of jaundice. This can happen when the mother has Rh-negative blood and the baby has Rh-positive blood.

3. Previous sibling with jaundice: If a baby has a sibling who had jaundice as a newborn, there is a higher likelihood of developing jaundice as well.

4. Bruising during birth: Babies who experience bruising or trauma during the birthing process may have an increased risk of jaundice due to the breakdown of red blood cells.

5. Breastfeeding difficulties: Babies who have trouble breastfeeding in the first few days of life may be at a higher risk of developing jaundice.

6. East Asian or Mediterranean descent: Babies of East Asian or Mediterranean descent are more prone to developing jaundice due to a higher prevalence of certain genetic factors.

7. Genetic conditions: Certain genetic disorders can affect the liver's ability to process bilirubin effectively.

8. Infection during pregnancy or after birth: Infections can disrupt liver function and contribute to jaundice.

9. Difficulties with breastfeeding: Inadequate milk intake can lead to dehydration and increased bilirubin levels.

10. Excessive weight loss in the baby: Significant weight loss can result in increased bilirubin levels.

11. Certain medications taken by the mother during pregnancy: Some medications can affect the baby's liver function.

12. Blood disorders, such as G6PD deficiency: These disorders can cause an increase in bilirubin production.

13. Liver disease: Any liver condition that impairs bilirubin processing can contribute to jaundice.

14. Hypothyroidism in the baby: An underactive thyroid can affect bilirubin metabolism.

15. Maternal diabetes: Babies born to diabetic mothers have a higher risk of developing jaundice.

16. Rh disease: Incompatibility between the mother's and baby's blood types can lead to jaundice.

17. Male gender: Boys are more likely to develop jaundice than girls.

18. Blood group O: Babies with blood group O are at a slightly higher risk of jaundice.

19. Maternal age over 25: Older mothers may have an increased risk of neonatal jaundice.

20. Prolonged labour or difficult delivery: Trauma from a difficult birth can contribute to jaundice.

21. Family history of jaundice: If there's a history of jaundice in the family, the baby may have a higher risk.

DIAGNOSIS

When it comes to diagnosing neonatal jaundice, healthcare professionals follow a systematic approach to determine the cause and severity of the condition. Let's dive into the diagnosis process.

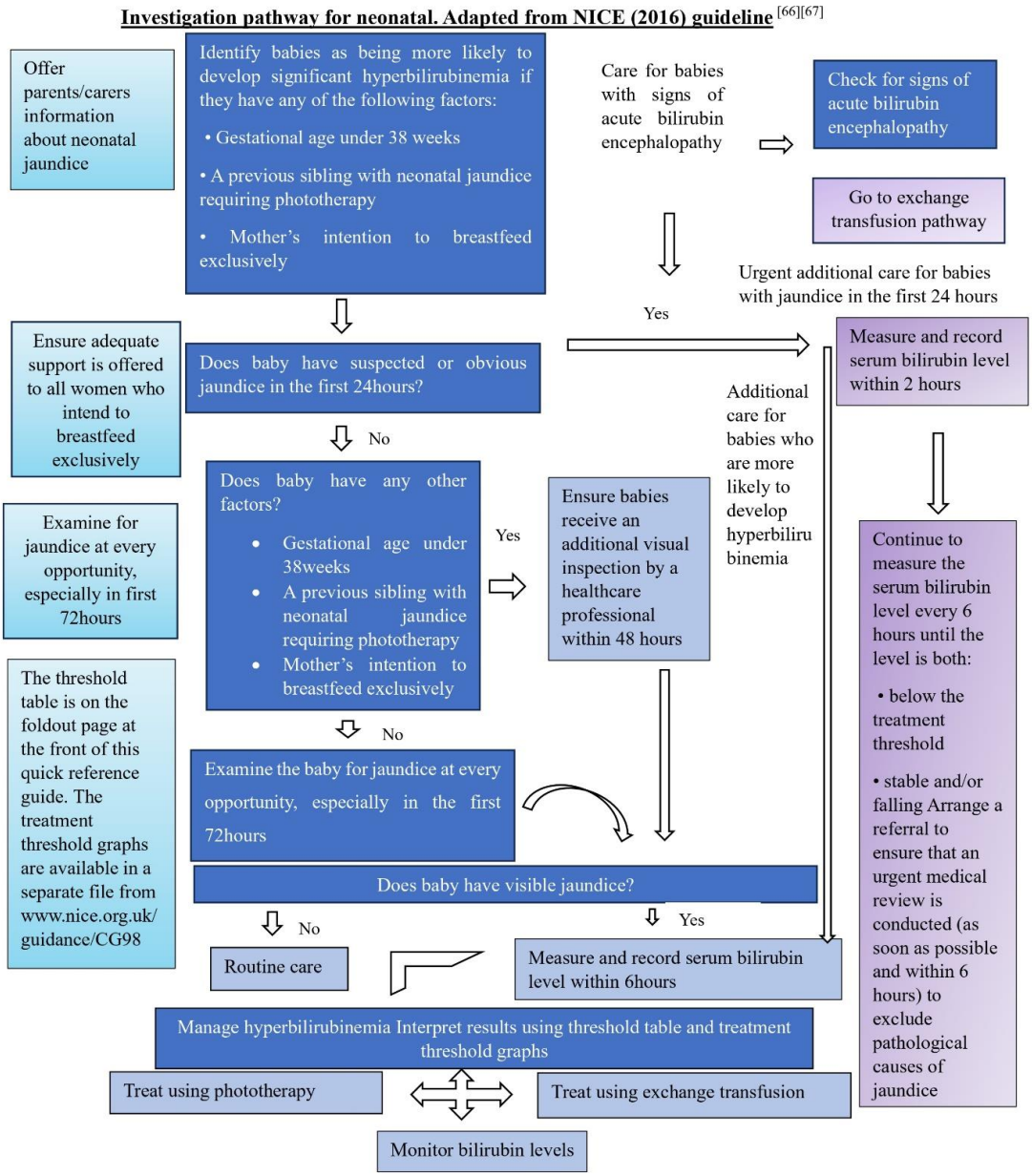
1. Physical Examination: The first step is a thorough physical examination of the baby. The healthcare provider will assess the baby's skin color, particularly looking for yellowing or jaundice in the eyes, face, and body. They may also check for any other signs or symptoms that could indicate an underlying condition.[68][69]

2. Bilirubin Level Measurement: The next step is to measure the baby's bilirubin levels. This can be done using a non-invasive device called a transcutaneous bilirubinometer, which measures the bilirubin levels by shining a light on the baby's skin. In some cases, a blood test may be required to obtain a more accurate measurement.[70][71]

3. Risk Assessment: Based on the bilirubin levels and the baby's overall health, the healthcare provider will assess the risk factors associated with neonatal jaundice. These risk factors include prematurity, blood type incompatibility, previous siblings with jaundice, and certain ethnic backgrounds.[71][72]

4. Additional Tests: Depending on the findings from the physical examination and risk assessment, further tests may be recommended. These tests can include blood tests to determine the specific type of jaundice, such as a complete blood count (CBC) and blood group testing. Other tests, like a Ultrasound scan, a urine sample for infection testing, a reticulocyte counts , exploratory surgery (rarely) and Coombs test, may be performed to check for antibodies that could be causing hemolytic jaundice.[73][74]

5. Monitoring: Once the diagnosis is made, the baby's bilirubin levels will be closely monitored to track the progression of jaundice. This can be done through regular follow-up appointments and bilirubin level checks. Monitoring is important to ensure that the bilirubin levels do not reach dangerous levels that could potentially harm the baby's brain.[75][76]



MANAGEMENT

Medical intervention is usually necessary when the bilirubin level in the child's blood is elevated. In certain cases, symptoms are present, but the bilirubin level in the blood is low, and no therapy is required. In these circumstances, the symptoms will improve within 10-14 days, and the baby should be regularly breastfed or bottle-fed, causing no harm to the body.[69]

Jaundice is a common condition in newborns that can be managed through various treatments depending on the cause of the condition, bilirubin levels, and the age of the baby.

1. Enhanced nutrition

It can be accomplished by using More frequent feedings or supplemental feeding. Typically, it is advised to avoid losing weight.[3]

More frequent feeding

A frequently fed infant obtains more milk, resulting in more bowel movements and bilirubin in the baby's feces. Breastfed newborns should have 1 to 2 ounces (or 30 to 60 milliliters) of breast milk every 2-3 hours for the first week.[77]

Supplemental feedings

If the infant has trouble breastfeeding, loses weight, or is dehydrated, formula or expressed milk can be used to supplement breastfeeding. The doctor may advise temporarily discontinuing nursing and then restarting it.[78]

2. Phototherapy

Phototherapy is an effective treatment for neonatal jaundice that involves exposing the newborn’s skin to light that emits light in the blue-green spectrum.[3] This light helps the liver break down bilirubin and remove it from the blood. During the treatment, the infant is placed in an incubator under the light, wearing only a diaper and eye patch.[79]

The neonate’s temperature is monitored, and every 30 minutes, a break is made to feed and change the diaper. Bilirubin levels are checked every 4 to 6 hours to assess the effectiveness of the therapy.[80]

If jaundice persists, enhanced phototherapy may be provided by increasing the amount of light or simultaneously using another light source, such as a light blanket.[81]

3. Exchange transfusion

In cases where phototherapy fails to achieve the desired results, a complete blood transfusion may be deemed necessary.

During an exchange transfusion, a plastic tube is inserted into the baby's umbilical cord, arms, or legs to collect blood from the infant. Blood of the same or a similar blood type is then used to replace the original blood.[82][83] The absence of bilirubin in the fresh blood leads to a rapid decrease in the total bilirubin level in the baby's blood. The process is repeated if

the bilirubin level remains high. The transfusion procedure is closely monitored by medical personnel and it takes several hours.[84][85]

Any complications that arise, such as bleeding, are promptly addressed. The infant's blood is evaluated within two hours of treatment to assess the efficacy of the procedure. If the bilirubin level remains high, the procedure may be repeated.[86]

4. Intravenous immunoglobulin (IVIg)

Jaundice may be caused by blood group discrepancies between the mother and neonate. This is because the infant acquires maternal antibodies that rapidly break down the infant's red blood cells.[87]

An intravenous infusion of immunoglobulin, a blood protein that can lower antibody levels, may eliminate the need for an exchange transfusion.[75]

Treatment for jaundice is typically required if an underlying medical condition, such as an infection, is the cause. Intravenous immunoglobulin (IVIG) may be used if rhesus illness is responsible for jaundice, which occurs when the mother has rhesus-negative blood, and the newborn has rhesus-positive blood.[76]

IVIG is typically used when phototherapy alone is ineffective, and the blood bilirubin level is still rising.[88]

The best way to reduce an infant's risk of developing jaundice is to ensure that they receive adequate nutrition. Infants who are breastfed should be fed 8-12 times daily during their first week of life, while those who are formula-fed should receive 1-2 ounces of formula every two to three hours.[77][89]

If the baby's condition worsens, or the symptoms do not go away after 2 weeks, it's important to seek the help of a medical professional such as a midwife, GP, maternal and child health nurse, pediatrician, or call the Maternal and Child Health Line (24 hours) at 1098 for assistance.[90]

CONCLUSION

While neonatal jaundice is common and usually benign, early detection and appropriate management are vital to prevent severe complications. Continued research and education are

essential to optimize outcomes for affected infants. Healthcare providers must grasp the etiology, risk factors, and clinical manifestations of neonatal jaundice for early diagnosis and proper management. Ongoing research and advances in treatment strategies offer promise for further decreasing the incidence and severity of severe neonatal jaundice, thereby enhancing neonatal health outcomes globally.

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