EJPMR, 2026, 13(3), 484-493 **Review Article** **Impact Factor 8.158**

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

ISSN (O): 2394-3211
ISSN (P): 3051-2573
Coden USA: EJPMAG

A REVIEW ON NEONATAL JAUNDICE

Saroj Kumari*[1], Raman Gupta[2], Dr. Jyoti Gupta[3], Shalu Dhiman[2], Yashsavi Bali[2]

[1]IEC School Pharmacy, IEC University, Kalujhanda, Baddi, Solan, Himachal Pradesh, 174103.
[2]Associate Professors IEC School of Pharmacy, IEC University, Kalujhanda, Baddi, Solan, Himachal Pradesh, 174103.
[3]HOD, IEC School of Pharmacy, IEC University, Kalujhanda, Baddi, Solan, Himachal Pradesh, 174103.

***Corresponding Author: Saroj Kumari**

IEC School Pharmacy, IEC University, Kalujhanda, Baddi, Solan, Himachal Pradesh, 174103.

DOI: https://doi.org/10.5281/zenodo.18937694

How to cite this Article: Saroj Kumari*[1], Raman Gupta[2], Dr Jyoti Gupta[3], Shalu Dhiman[2], Yashsavi Bali[2] (2026). A Review On Neonatal Jaundice. European Journal of Pharmaceutical and Medical Research, 13(3), 484–493.

Article Received on 15/02/2026 **Article Revised on 05/03/2026** **Article Published on 10/03/2026**

ABSTRACT

Neonatal jaundice is among the most common medical problems that babies in the neonatology department face. Basically, it is a condition that results from an excessive accumulation of bilirubin, which is a yellow pigment released by the breakdown of red blood cells in the baby's body. It has been reported that 60% of full-term and 80% of preterm neonates develop visible jaundice within the first week of their life (NeoReviews, 2020; Medscape, 2024). Typically, this condition is the result of normal physiological changes during the transition after birth, and it normally goes away without any treatment (StatPearls, 2023). However, some infants with jaundice may develop very high levels of bilirubin leading to pathological jaundice that necessitates immediate medical treatment (Hansen, 2021). The study of neonatal jaundice is important due to its paradoxical nature — it can either be a normal physiological process or a potentially fatal disorder based on its etiology and severity (IJHMR, 2024). Hence, gaining knowledge about its pathophysiology, identification, and treatment is essential for promoting infant health and minimizing disease and death.

KEYWORDS: Neonantal Jaundance, Physiology, Biochemistry, Etiology, Pathophysiology, Diagnosis.

INTRODUCTION

His Infant jaundice has been recognized since ancient times. Hippocrates was the first to refer to newborns with yellow discoloration (Hansen, 2021). The present-day knowledge of bilirubin metabolism only took shape after the 20th century when phototherapy was discovered as a treatment method in the 1950s by Cremer et al., who found that sunlight helps in reducing jaundice in babies (Bhutani et al., 2011). From simply exposing infants to sunlight, the treatment of neonatal jaundice has seen a remarkable change to the present-day techniques of highly efficient LED phototherapy and non-invasive transcutaneous bilirubin measurement (Medscape, 2024; MDPI, 2023). Besides, the identification of bilirubin-binding proteins and molecular pathways has further enlightened us on the disease process (Hansen, 2021).

Bilirubin is a waste product formed when the body breaks down heme, mainly as a result of red blood cells being destroyed.

Bilirubin Metabolism Pathway

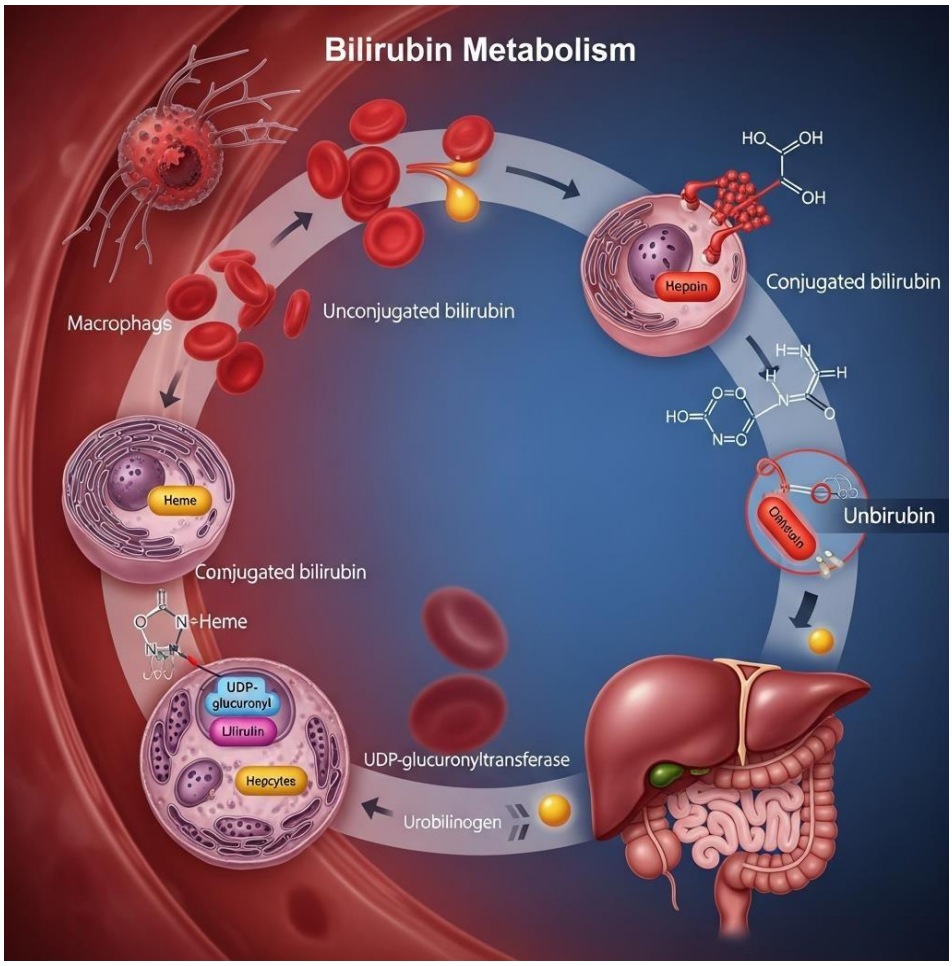
Production: Most (about 75%) of the bilirubin is derived from the breakdown of haemoglobin in red blood cells and the rest is from ineffective erythropoiesis and the destruction of other heme-containing proteins. (Hyperbilirubinaemia review, 2016).

Transport: The unconjugated (indirect) bilirubin produced is a lipid-soluble molecule and so it is tightly bound by plasma albumin for safe transport through the blood plasma to the liver for processing (Medscape, 2024).

Conjugation: Once in the hepatocytes, the enzyme UDP-glucuronyl transferase transforms lipid-soluble unconjugated bilirubin into water-soluble conjugated bilirubin by coupling it with glucuronic acid, which makes its excretion easier (AAFP, 2023).

Excretion: The conjugated bilirubin is exported with bile into the intestine, where it is broken down by the

intestinal bacteria into urobilinogen and stercobilin which are eliminated in urine and feces respectively (IJHMR, 2024).



The enzyme responsible for conjugation is immature in neonates, thus, unconjugated bilirubin keeps increasing, which is capable of crossing the blood–brain barrier and causing toxicity (NeoReviews, 2020).

Neonatal jaundice causes can be classified into two main groups i.e., physiological and pathological jaundice with each having distinct characteristics like underlying cause, time of onset and severity.

Physiological jaundice is essentially a normal phenomenon that most healthy newborns experience as a result of an immature liver and the rapid breakdown of fetal red blood cells. It generally occurs from the 2nd to 4th day of life, reaches its peak on the 5th day, and goes away by the 10th to 14th day without treatment (StatPearls, 2023). On the other hand, pathological jaundice that either appears in the first 24 hours of life or lasts for more than two weeks usually is caused by haemolytic disease, infections or metabolic disorders and thus, requires medical treatment (AAFP, 2023).

Physiological Jaundice

It's a type of jaundice that happens when the liver of a newborn is not fully equipped to remove the bilirubin from the blood efficiently hence the buildup of the yellow pigment in the baby's organs and body tissues.

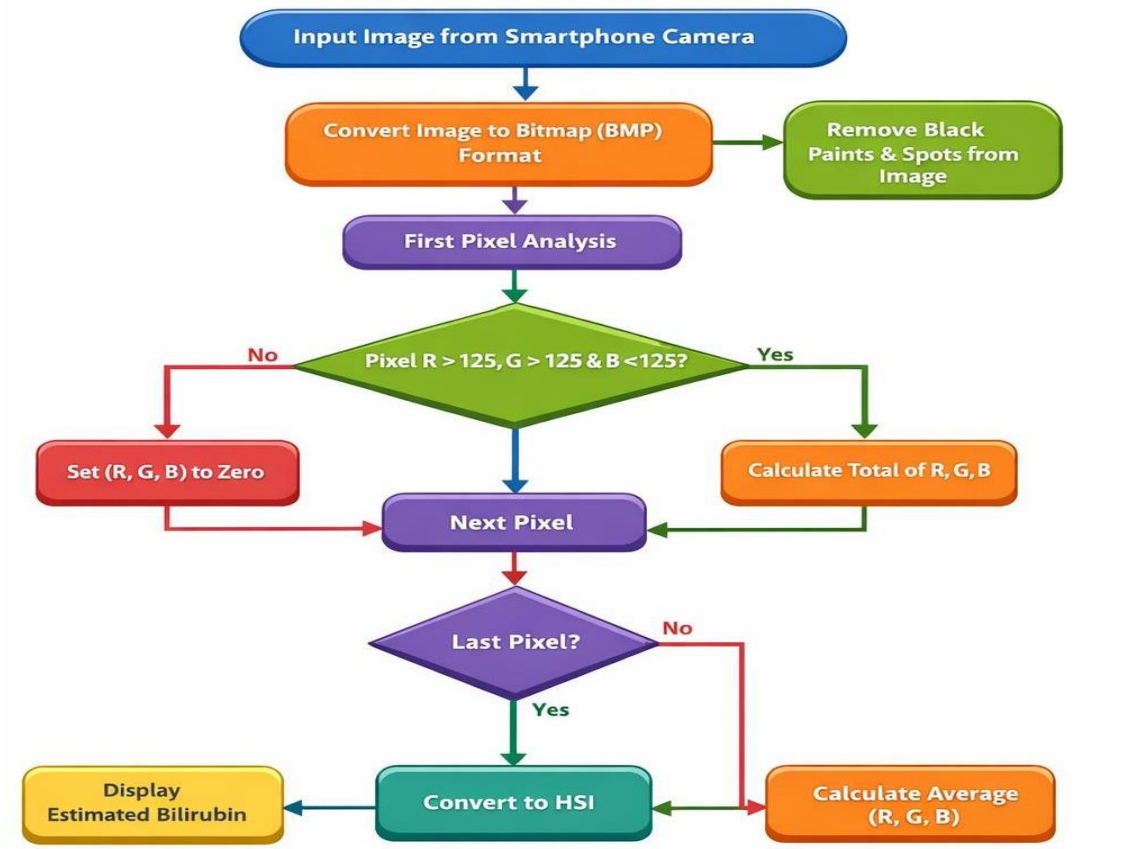
Physiological jaundice is normal and harmless but like with everything else, overdoing is harmful hence if the bilirubin levels go beyond 15 mg/dl, there can be a problem and this calls for more tests. It usually appears between days 2 and 4 after birth and disappears within two weeks without the need for medication or other interventions. The figure below shows a baby with physiological jaundice.

Other types of neonatal jaundice include pathological causes, which result from underlying diseases and require prompt treatment. Some of the common causes are.

- Haemolytic diseases (e.g., Rh or ABO incompatibility): This situation arises when an immune reaction happens between a mother's and a baby's blood types. In Rh incompatibility, an Rh-negative mother produces antibodies against the Rh-positive red blood cells of her baby thereby destroying them and releasing excessive bilirubin. ABO incompatibility occurs when a mother with blood group O carries with mother group A or B resulting in mild to moderate haemolysis. Both are associated with the rapid buildup of bilirubin shortly after

birth, usually within the first 24 hours (Medscape, 2024).

- Infections (Sepsis or TORCH infections): Infection like sepsis (generalised bacterial infection) or TORCH infections (Toxoplasmosis, Others such as syphilis, Rubella, Cytomegalovirus, and Herpes simplex) can directly cause liver cell or red blood cell damage and thus bilirubin metabolism is impaired. Furthermore, the infections may lower liver enzyme activity leading to either conjugated or mixed hyperbilirubinemia. Clinically the patient would present with other signs such as fever, refusal to feed and lethargy (AAFP, 2023).
- Prematurity (Immature liver function): A premature baby has immature liver enzyme systems and low albumin levels necessary to bind and process bilirubin. Therefore, only a slight increase in bilirubin production will result in a considerable increase in blood levels. As a result, premature babies have a higher risk of severe hyperbilirubinemia and kernicterus compared to term babies (StatPearls, 2023).
- Genetic disorders (G6PD deficiency, Crigler–Najjar syndrome): Some hereditary diseases interfere with the normal process of bilirubin metabolism. For instance, G6PD deficiency mellows the red blood cells causing them to break more easily and thus overflow of bilirubin happens, this is more severe when there is also infection or certain drugs, Crigler-Najjar syndrome is an extremely rare inherited disorder in which the enzyme UDP-glucuronyl transferase is absent or defective leading to impaired bilirubin conjugation and as a result, high unconjugated bilirubin levels are persistently present (Hansen, 2021).
- Metabolic causes (Hypothyroidism, Galactosaemia): In congenital hypothyroidism, a decreased thyroid hormone level slows bilirubin conjugation and liver metabolism. Galactosaemia is a rare inherited disease that leads to the build-up of toxic substances in the liver which interfere with bilirubin excretion. Both conditions are associated with prolonged jaundice beyond the usual neonatal period (IJHMR, 2024).
- Breast milk jaundice (due to inhibitory substances in breast milk): This condition comes in healthy breast-fed babies after the first week of life. Certain components in breast milk, such as β-glucuronidase or free fatty acids, inhibit bilirubin conjugation or facilitate intestinal reabsorption. Bilirubin levels might be still mildly elevated for several weeks, but the baby usually grows normally and no treatment is required except for monitoring and continued breastfeeding (Women, Midwives & Midwifery, 2023).



Classification

The classification of neonatal jaundice is based on its cause, time of onset, and duration. It helps differentiate between normal physiological processes and conditions that require medical attention.

The main types are summarised below.

Type	Timing of Onset	Cause	Duration	Example
Physiological	2–4 days after birth	Normal adaptation	≤ 2 weeks	Common in healthy newborns
Pathological	Within 24 hours	Disease-related	> 2 weeks	Hemolytic jaundice
Breastfeeding jaundice	2–5 days	Poor milk intake	Variable	Dehydration-related
Breast milk jaundice	1–2 weeks	Breast milk substance	May persist for 1–2 months	Benign

Clinical Features

A yellowish discoloration of the skin and the white part of the eyes (sclera) is the landmark sign of neonatal jaundice which results from an increase in bilirubin levels in the blood (NHS, 2024). This yellow tone usually first shows on the face and scalp, then slowly moves downward to the chest, tummy, arms and finally the legs and soles as the level of bilirubin gets higher — this is called the cephalocaudal progression (Hansen, 2021).

Along with the visible yellowing, a couple more symptoms may suggest that the jaundice is more than just the physiological.

- Poor feeding: Babies with the condition might be reluctant to breastfeed or have a weak suction, resulting in dehydration and exacerbation of jaundice.
- Lethargy: The infant can seem very sleepy, hard to wake or inactive — all of which can be signs of bilirubin toxicity to the brain.
- High-pitched crying: A shrill or piercing cry might indicate bilirubin encephalopathy which is a severe neurological condition.
- Dark urine and pale (clay-coloured) stools: In cases of cholestatic or obstructive jaundice, the passage of bilirubin into the intestine is blocked which causes dark urine (bilirubin in urine) and pale stools (due to the absence of bile pigment).
- Signs of encephalopathy (in severe cases): Extremely high bilirubin levels can make it pass through the blood–brain barrier and have a degenerative effect on the brain tissue. These signs include low muscle tone (hypotonia), seizures, body backward arching (opisthotonus), and if not treated, coma (AAFP, 2023)

Diagnosis

Physical Examination

The Kramer's rule helps estimate bilirubin levels by observing the area of yellow discoloration.

Zone	Area	Approx. Serum Bilirubin (mg/dL)
1	Face and neck	5
2	Chest and upper abdomen	5–8
3	Lower abdomen and thighs	8–12
4	Arms and lower legs	12–15

Laboratory Tests

1. – Serum bilirubin estimation (total and direct/conjugated). (Medscape, 2024)
2. – Blood group and Coombs test (for haemolysis). (AAFP, 2023)
3. – Complete blood count (CBC). (IJHMR, 2024)
4. – Reticulocyte count. (Hyperbilirubinaemia review, 2016)
5. – Liver function tests. (Medscape, 2024)
6. – Serum bilirubin estimation (total and direct/conjugated). (Medscape, 2024)
7. – Blood group and Coombs test (for haemolysis). (AAFP, 2023)
8. – Complete blood count (CBC). (IJHMR, 2024)
9. – Reticulocyte count. (Hyperbilirubinaemia review, 2016)
10. – Liver function tests. (Medscape, 2024)

Evaluation of Neonatal Jaundice – Reformated Table

Step 1: Identify the Type of Hyperbilirubinemia	
Direct (Conjugated) ↑	Liver or bile flow disease
Indirect (Unconjugated) ↑	Hemolysis, immaturity, or increased RBC breakdown

A. Causes of Increased Direct (Conjugated) Bilirubin	
Step 1 – Direct Coombs Test	
Positive	Isoimmunization (Rh, ABO), other blood group ecompatibility incompatibility
Negative	Proceed to hemolobin level

B. Evaluation of Increased Indirect (*Unconjugated*) Bilirubin

Step 1 – Direct Coombs Test	
Positive	Proceed to hemglobin level
High (Polycythemia) • Twin-twin tranfusion • Maternal-fetal transfynic • Giant cell hepatitis	Twin-twin transfusion Maternal-fetal transfusion Delayed cord clamping Small for gestational age
Normal or Low	Check reticulocyte count

Step 3 - Reticulocyte Count

Increased	**Increased**	Ongoing hemolysis → examine RBC morphology
Normal	Consider non-hem	Consider non-hemolytic causes

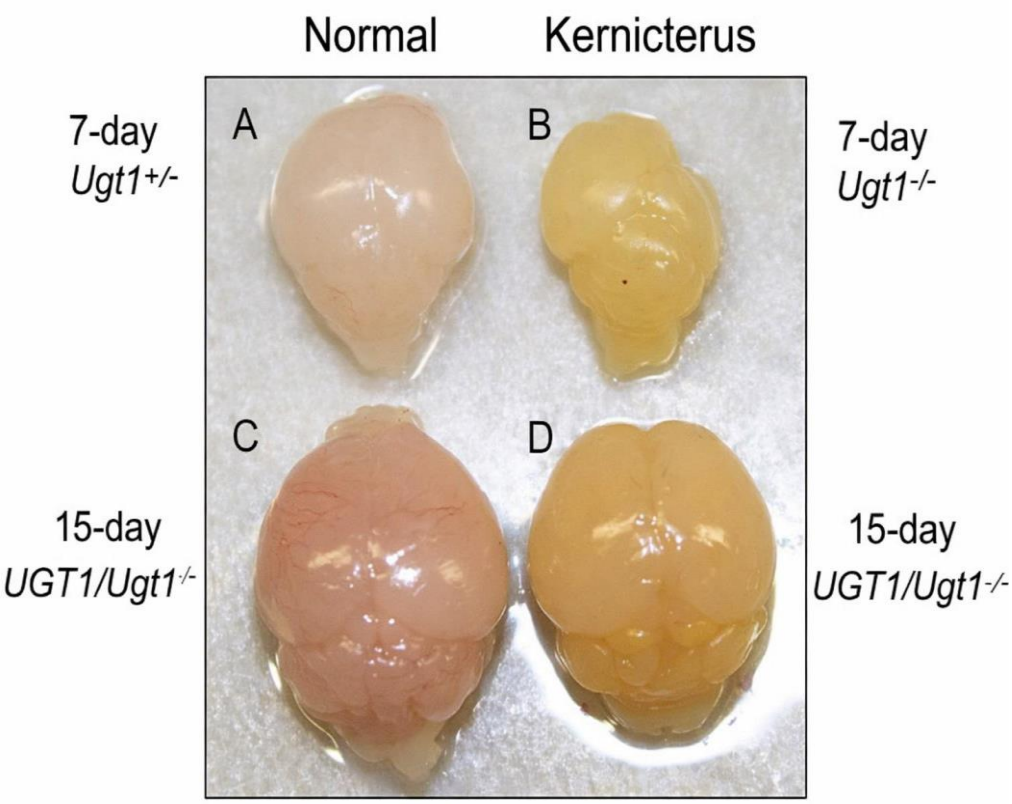
Step 4 - Red Cell Morphology

Pattern	**Pattern**	**Normal**
Pattern	**Characteristic cells** • Spherocytosis • Elliptocytosis • Stomatocytosis • Pyknocytosis • Fragmented cells	Enclosed hemorrhage ↑ enterohepatic circulaton Delayed/infrequent stooling Bowel obstruction Poor caloric intake Neonatal asphyxia
Nonspecific	G6PD G6PD deficiency Pyruvate kinase deficiency Other enzyme defects DIC	Enclosed hemorrhage ↑ enterohepatic circulation Delayed/infrequent stooling Bowel obstruction Neonatal asphyxia

C. Causes of Prolonged Indirect Hyperbilirubinemia

Pathophysiology of Hyperbilirubinemia

- Newborns normally have two types of bilirubin: unconjugated (indirect) and conjugated (direct), each kind having distinct clinical significance (NeoReviews, 2020)
- Unconjugated bilirubin is the component released after red cells were lysed. It remains unprocessed by liver and is still liposoluble. Liver enzymes in neonates, especially preterm babies, are still immature, thus, the capacity to transform this unconjugated bilirubin into a water-soluble form is very limited. Hence, unconjugated hyperbilirubinaemia (high level of unconjugated bilirubin) is very common in healthy neonates for the first 72 hours and is usually physiological (StatPearls, 2023). Nevertheless, if the level is extremely elevated, the condition might be critical (AAFP, 2023). Conversely, conjugated bilirubin is the one that yeast through UDP-glucuronyl transferase enzyme activity (a cofactor liver) which attaches gluturonic acid to bilirubin and converts it into a water- soluble form and hence excretion in bile. Hence, conjugated (direct) bilirubin levels are elevated inpathological conditions only, as it denotes a situation where the liver is synthesizing conjugated bilirubin but cannot eliminate it.
- The frequently seen disorders of bile flow include biliary atresia, hepatitis, metabolic or genetic liver diseases, and obstruction of bile flow (Medscape, 2024).



Treatment and Management of Neonatal Jaundice

Neonatal jaundice treatment primarily aims to lower blood bilirubin levels and protect the brain from bilirubin-induced damage such as kernicterus. The appropriate therapy depends on the kind, severity, etiology, and age of the infant (AAFP, 2023). It may comprise mainly supportive care measures, phototherapy, exchange transfusion, and drug therapy.

General Care

Regardless of the etiology or intensity, basic supportive care is very important for all infants with jaundice.

- Ensure feeding and hydration: Frequent breastfeeding (8-12 times a day) helps stimulate defecation, which promotes bilirubin elimination via feces. Inadequate feeding can lead to an increase in bilirubin reabsorption from the gut, thus worsening jaundice. If the infant does not take enough food by mouth, dehydration can be prevented by administering fluids intravenously (IJHMR, 2024).
- Avoid using displacing bilirubin from albumin drugs: Some medicines (e.g., sulfa drugs, ceftriaxone, aspirin) may displace bilirubin from its albumin binding site resulting in an increase in free (unbound) bilirubin in the circulating blood. Such drugs should be avoided during the neonatal period to prevent bilirubin toxicity (Hyperbilirubinaemia review, 2016).

These five simple general care measures assist the infant's metabolism and thus, mild jaundice can resolve naturally without complications.

Phototherapy

- Phototherapy is the primary and a very widely used method for newborn jaundice. It is a non-invasive, safe, and quite effective method whereby light energy is used to convert the bilirubin into excretable forms (StatPearls, 2023).
- Mechanism: Blue light of 460 nm wavelength is used since it corresponds to the bilirubin absorption maximum. The light penetrates the skin and causes photo-isomerisation and structural isomerisation of bilirubin which is converted to lumirubin and other water-soluble products that can be eliminated via urine and bile even without the action of the liver (AAFP, 2023).

Phototherapy Unit Types

1. Conventional fluorescent lamps: These were the first phototherapy devices but are more energy- consuming and generate more heat compared to modern devices.
2. Compact fluorescent (CFL) lamps: Provide better light intensity and more uniform light distribution as compared to traditional tubes.
3. LED phototherapy units: The newest, and most effectively energy-efficient, method is based on light-emitting diodes that provide precise blue lights, use less power, produce less heat and last longer (MDPI, 2023).

Phototherapy Side Effects: Phototherapy is normally a safe therapeutic measure though it can sometimes cause minor side-effects such as.

4. Loss of water through the skin resulting in dehydration.
5. After light exposure, the skin might have slight redness or rashes.
6. Depending on the ambient temperature and duration

of exposure, the infant may either become too hot or too cold.

7. Bronze baby syndrome is a very rare disorder mainly affecting infants with conjugated hyperbilirubinemia, whereby skin color becomes grayish-brown during therapy (Spandidos Publications, 2021).

Continuous monitoring of the baby's temperature, hydration, and bilirubin levels is an essential strategy to prevent the development of complications during treatment.

Exchange Transfusion

Exchange transfusion is a drastic and potentially life-saving step typically reserved for extremely high bilirubin levels, especially if total serum bilirubin is around 20 mg/dL (considering age and weight) or when jaundice is resistant even after using very intensive phototherapy (AAFP, 2023).

Purpose This procedure quickly gets rid of the excess bilirubin, maternal antibodies and sensitised red blood cells in the baby's blood stream thus stopping haemolysis and lowering the risk of kernicterus (StatPearls, 2023).

Procedure Steps

- Blood group matching and cross-matching: In order to prevent transfusion reactions, donor blood that is compatible with both mother and baby is selected.
- Umbilical vein catheterisation: For the purposes of blood removal and replacement, a catheter is inserted in the umbilical vein using sterile technique.
- Sequential exchange: Small amounts of the baby's blood are gradually removed and replaced with equal volumes of donor blood, usually totalling 160–180 mL per kilogram of body weight (AAFP, 2023).
- Possible risks and complications: Besides its high effectiveness, exchange transfusion is not without risks, which include infection, electrolyte imbalance, hypocalcaemia, hypoglycaemia, air embolism, and cardiac arrhythmias. For this reason, it is used only when absolutely necessary (StatPearls, 2023).

Complications

The bilirubin pigment is a byproduct of the degradation of hemoglobin in red blood cells and is normally processed by the liver. High and untreated levels of neonatal jaundice may cause dangerous complications when the bilirubin builds up in the blood to the point where it starts affecting the brain and the nervous system.

The most serious Complications of neonatal jaundice include acute bilirubin encephalopathy (ABE) and kernicterus, which are two different stages of brain damage caused by high levels of bilirubin (AAFP, 2023).

- Acute Bilirubin Encephalopathy (ABE): This is the initial and potentially reversible stage of bilirubin toxicity in the brain. When unconjugated bilirubin levels go very high, the pigment crosses the immature blood–brain barrier and accumulates in specific regions of the brain such as the basal ganglia, hippocampus and brainstem nuclei. At this stage, the baby may exhibit signs of illness such as poor feeding, extreme sleepiness (lethargy), a high-pitched or shrill cry, irritability, and decreased muscle tone (hypotonia). With prompt and aggressive treatment (usually through intensive phototherapy or exchange transfusion) the effects of ABE can often be reversed, preventing permanent neurological damage (AAFP, 2023).
- Kernicterus: Kernicterus is the long-term and irreversible form of bilirubin-induced brain injury that results when ABE is not treated in time. In this stage, bilirubin causes permanent damage to neurons in the brain, especially in the globus pallidus and subthalamic nuclei, resulting in long-term neurological problems. Children who have this condition may have sensorineural hearing loss (deafness), cerebral palsy, abnormal muscle tone or movement disorders, impaired coordination, and developmental delays.

Kernicterus is a preventable condition, but it is permanent and can severely affect the child's quality of life once it is established (AAFP, 2023).

- Seizures and Hypotonia: As bilirubin toxicity advances, the infant might start having seizures caused by inflammation and brain damage. The baby could also develop hypotonia (floppy or weak muscles) or sometimes hypertonia (stiff, rigid muscles). These symptoms point to severe central nervous system involvement and require immediate medical attention (StatPearls, 2023).
- Death (in extreme cases): Death can occur if hyperbilirubinaemia is not treated and the brain is damaged by bilirubin to such an extent that the respiratory system is compromised, the patient falls into a coma, and eventually dies. However, this sad case is quite rare nowadays because neonatal jaundice is regularly checked and treated in good time (AAFP, 2023).

Prognosis

The majority of physiological jaundice cases are completely resolved naturally. When conventional treatment is applied, the outcome is almost always good (StatPearls, 2023). However, if pathological jaundice is left untreated, it may cause serious brain damage or neurological sequelae (AAFP, 2023). A combination of neonatal screening, advancements in phototherapy technology, and greater awareness has led to a dramatic decrease in severe hyperbilirubinaemia and kernicterus cases worldwide (BMJ Paediatrics Open, 2017).

Recent Advances and Research

Over the past decade, several new technologies have enhanced neonatal jaundice diagnosis and treatment, thus making the methods safer, more accurate and broadly available.

- LED-based Phototherapy Units: Traditional fluorescent lamps have been replaced by LED phototherapy. These LEDs emit specific blue wavelength

(~460 nm) which efficiently degrades bilirubin and at the same time generates less heat and uses less energy. Besides that, they are more rugged, small and very handy even in the under-equipped or remote area healthcare facilities (MDPI, 2023).

- Transcutaneous Bilirubinometry (TcB): TcB is a device that uses light reflectance technology through the skin to measure bilirubin non-invasively. With this device, getting results is fast, easy and accurate, at the same time, it limits the need for frequent phlebotomy and helps in the early diagnosis of jaundice in infants (Hansen, 2021).
- Genetic Research: By studying genes such as UGT1A1 and G6PD, scientists have lately recognized that these genes affect how bilirubin is metabolized in the body and that they can lead to severe jaundice. Determining these genetic components can be very helpful in the identification of newborns who are at risk of developing high levels of bilirubin and therefore, the intervention and monitoring can be done timely (IJHMR, 2024).
- Home Phototherapy Units: In cases of mild jaundice where there are no complications, the use of portable home phototherapy units which operate on LED lights is a good way of allowing the patients to be treated at home with medical supervision. Research indicates that, this method can lead to savings in costs and also be very convenient, besides it can be helpful in limiting the number of cases that require hospital admission especially in remote areas (MDPI, 2023).
- Artificial Intelligence (AI) Models: It is a fact that AI and machine-learning algorithms are being devised to estimate the likelihood of severe jaundice using newborn information including birth weight, gestational age, and bilirubin levels. Apps running AI on smartphones are even capable of helping identify jaundice through visual means, thus facilitating early screening even at home or in local medical facilities (MDPI, 2023).

CONCLUSION

Neonatal jaundice is still very much a concern in newborn care due to its high frequency and the potential for serious complications if it is neglected or improperly managed. It may be a physiological process that occurs in the majority of infants normally, yet without proper monitoring and intervention, the danger is that bilirubin will still accumulate to levels high enough to cause neurological damage like kernicterus or even death. Hence, early detection, proper diagnosis, and expedient treatment play vital roles in averting disability in the long run and in lowering infant morbidity and mortality. The condition is a warning of how a seemingly innocuous and ordinary neonatal occurrence can rapidly change into a life-threatening emergency if it is ignored.

Continuous advancements in medical technology, neonatal screening, and parental education have significantly contributed toward the high survival rate of infants with severe complications that are now almost non-existent. Research and technological breakthroughs such as LED phototherapy, non-invasive monitoring, and genetic screening are not only raising awareness but also helping to better the management of neonatal jaundice globally.

REFERENCES

1. Hansen, T.W.R., 2021. Narrative review of the epidemiology of neonatal jaundice. *Pediatric Medicine*, 4(18).
2. Maisels, M.J. and McDonagh, A.F., 2008. Phototherapy for Neonatal Jaundice. *New England Journal of Medicine*, 358(9): 920–928.
3. American Academy of Pediatrics (AAP): 2022. Management of Hyperbilirubinemia in the Newborn Infant 35 or More Weeks of Gestation. *Pediatrics*, 150(3): e2022058859.
4. Bhutani, V.K. et al., 2011. Neonatal Hyperbilirubinemia and Kernicterus: Causes and Prevention. *Pediatrics*, 128(4): e1046–e1052.
5. Cremer, R.J., Perryman, P.W. and Richards, D.H., 1958. Influence of light on the hyperbilirubinemia of infants. *The Lancet*, 271(7030): 1094–1097.
6. Kliegman, R.M. et al., 2020. *Nelson Textbook of Pediatrics*. 21st ed. Philadelphia: Elsevier.
7. Slusher, T.M. et al., 2017. Burden of severe neonatal jaundice: a systematic review and meta-analysis. *BMJ Paediatrics Open*, 1: e000105.
8. Watchko, J.F. and Tiribelli, C., 2013. Bilirubin-induced neurologic damage — mechanisms and management approaches. *N Engl J Med*, 369(21): 2021–2030.
9. Gartner, L.M., 2011. Breastfeeding and jaundice. *Journal of Perinatology*, 31(S1): S25–S28.
10. Cloherty, J.P., Eichenwald, E.C. and Stark, A.R., 2012. *Manual of Neonatal Care*. 7th ed. Lippincott Williams & Wilkins.
11. Porter, M.L. and Dennis, B.L., 2002. Hyperbilirubinemia in the term newborn. *Am Fam Physician*, 65(4): 599–606.
12. Dennery, P.A., Seidman, D.S. and Stevenson, D.K., 2001. Neonatal hyperbilirubinemia. *N Engl J Med*, 344: 581–590.
13. Olusanya, B.O., Kaplan, M. and Hansen, T.W.R., 2018. Neonatal hyperbilirubinemia: A global perspective. *The Lancet Child & Adolescent Health*, 2(8): 610–620.
14. Neonatal Jaundice – StatPearls, 2023. *NCBI Bookshelf*. [online] Available at: https://www.ncbi.nlm.nih.gov/books/NBK532930/
15. Medscape, 2024. Neonatal Jaundice: Pathophysiology and Treatment. [online] Available at: https://emedicine.medscape.com/article/974786-overview
16. Hansen, T.W.R. and Wong, R.J., 2020. Neonatal Jaundice and Kernicterus. *J Clin Transl Hepatol*, 8(4): 441–450.
17. WHO, 2019. *Management of Hyperbilirubinaemia in Newborns*. Geneva: World Health Organization.
18. AAP NeoReviews, 2020. Indirect Hyperbilirubinemia in the Newborn. *NeoReviews*,

21(11): e749.
19. American Family Physician, 2023. Neonatal Hyperbilirubinemia: Evaluation and Treatment. *Am Fam Physician*, 107(5): 511–520.
20. International Journal of Health and Medical Research (IJHMR): 2024. Etiology, Pathophysiology and Management of Neonatal Jaundice. *IJHMR*, 10(3).
21. Women, Midwives and Midwifery Journal, 2023. Annisa, P. et al. Neonatal Jaundice Causal Factors: A Literature Review. *WMMJ*, 3(1): 45–60.
22. National Health Service (NHS): 2024. Newborn Jaundice. [online] Available at: https://www.nhs.uk/conditions/jaundice-newborn/.
23. MDPI Biosensors, 2023. Development of non-invasive LED-based phototherapy and bilirubin sensors. *Biosensors*, 14(5): 254.
24. Spandidos Publications, 2021. Challenges of phototherapy for neonatal hyperbilirubinemia (Review). *Exp Ther Med*, 21(2): 97.
25. Tiker, F., Gurakan, B. and Kilicdag, H., 2015. Risk factors for neonatal jaundice. *Pediatrics International*, 57(3): pp.516–521.
26. Olusanya, B.O. et al., 2020. Early identification of severe neonatal jaundice using transcutaneous devices. *Paediatrics & International Child Health*, 40(4): pp.222–230.
27. Maisels, M.J., 2015. Managing the jaundiced newborn: A persistent challenge. *Canadian Medical Association Journal*, 187(5): pp.335–343.
28. Kawade, N. and Onishi, S., 1981. The prenatal and postnatal development of UDP- glucuronyl transferase activity toward bilirubin. *Biochem J*, 196(1): pp.257–262.
29. Buchanan, R. and McCulloch, D., 2018. Neonatal sepsis and associated hyperbilirubinemia. *Clinical Neonatology Journal*, 22(2): pp.73–79.
30. Chaudhary, P. et al., 2019. Genetic polymorphisms in UGT1A1 and neonatal jaundice. *Indian Journal of Pediatrics*, 86(6): pp.517–523.
31. Kaplan, M. and Hammerman, C., 2020. Understanding G6PD deficiency and neonatal hyperbilirubinemia. *Seminars in Fetal and Neonatal Medicine*, 25(2): 101–118.
32. Bertini, G., Dani, C. and Pezzati, M., 2010. Prevention of bilirubin encephalopathy. *Journal of Maternal-Fetal & Neonatal Medicine*, 23(1): 67–69.
33. Watchko, J.F., 2016. Kernicterus and the molecular mechanisms of bilirubin neurotoxicity. *Pediatric Research*, 79(3): pp.473–479.
34. Agrawal, M. and Jain, S., 2017. Phototherapy and exchange transfusion in the management of neonatal jaundice: Review. *Indian J Neonatal Med Res*, 5(2): pp.9–15.
35. National Institute for Health and Care Excellence (NICE): 2016. *Jaundice in newborn babies under 28 days (CG98)*.
36. Kumar, P. and Chawla, D., 2015. Advances in neonatal phototherapy. *Indian Journal of Pediatrics*, 82(9): pp.744–751.
37. Mreihil, K., et al., 2018. Safety and efficacy of LED phototherapy in resource-limited settings. *BMC Pediatrics*, 18(1): 120.
38. Al-Lawama, M. et al., 2020. Evaluation of home phototherapy devices for neonatal jaundice. *Journal of Neonatal Nursing*, 26(6): pp.315–322.
39. Sgro, M. et al., 2016. Severe neonatal hyperbilirubinemia decreased after guidelines. *Pediatrics*, 138(3): e20154380.
40. Cohen, R.S. et al., 2018. Prevention of kernicterus. *Pediatrics*, 141(2): e20174067.
41. Stokowski, L.A., 2011. Fundamentals of phototherapy for neonatal jaundice. *Advances in Neonatal Care*, 11(S5): pp.S10–S21.
42. Agrawal, R., 2014. Neonatal hyperbilirubinemia: An update. *Journal of Neonatal Nursing*, 20(3): 115–125.
43. Kaplan, M. and Hammerman, C., 2002. Breast milk jaundice: A review. *Journal of Perinatology*, 22(7): pp.581–588.
44. Olusanya, B.O., Kaplan, M. and Hansen, T.W.R., 2021. Phototherapy in low-resource settings: strategies and innovations. *Semin Perinatol*, 45(5): 151464.
45. Ng, S.Y. and Chong, S.Y., 2020. Use of artificial intelligence for neonatal jaundice detection. *Frontiers in Pediatrics*, 8: 606–614.
46. Wong, R.J., Bhutani, V.K. and Stevenson, D.K., 2015. Molecular biology of bilirubin transport. *Semin Perinatol*, 39(3): pp.171–178.
47. Bhat, R.Y. et al., 2022. Risk factors for severe neonatal hyperbilirubinemia. *Pediatric Health, Medicine and Therapeutics*, 13: pp.89–97.
48. Stevenson, D.K. and Wong, R.J., 2019. Bilirubin neurotoxicity in the developing brain. *Semin Fetal Neonatal Med*, 24(1): pp.21–25.
49. Ghosh, S. and Mukherjee, R., 2018. Transcutaneous bilirubinometry in neonatal jaundice: Clinical utility. *Indian Pediatr*, 55(5): pp.403–409.
50. WHO, 2022. *Global Report on Newborn Health and Hyperbilirubinemia Management*. Geneva: WHO.
51. Almeida, M.F.B. et al., 2023. Innovations in neonatal jaundice management in developing countries. *Frontiers in Global Women's Health*, 4: 115.
52. Lauer, B.J. and Spector, N.D., 2011. Hyperbilirubinemia in the newborn. *Pediatrics in Review*, 32(8): pp.341–349.
53. Gartner, L.M., 2001. Kernicterus revisited. *Journal of Perinatology*, 21(Suppl 1): pp.S25–S28.
54. Bhutani, V.K., 2013. Evidence-based neonatal jaundice screening and treatment. *Pediatrics*, 132(4): pp.e1035–e1042.
55. Olusanya, B.O., Kaplan, M., and Hansen, T.W.R., 2019. Strategies to prevent severe neonatal hyperbilirubinemia. *Lancet Global Health*, 7(5): pp.e644–e652.
56. Chou, S.C. et al., 2020. Home phototherapy for neonatal jaundice: efficacy and safety. *Acta Paediatrica*, 109(3): pp.630–637.
57. Pediatric Research Society, 2022. Advances in

neonatal bilirubin metabolism research. *Pediatric Research*, 91(6): pp.1250–1258.
58. Yadav, S. and Gupta, N., 2021. Prevention and management of neonatal jaundice: A clinical update. *J Clin Neonatol*, 10(4): pp.203–210.
59. National Neonatology Forum of India (NNF): 2020. Guidelines on Neonatal Hyperbilirubinemia. *NNF Clinical Practice Guidelines*.
60. Karon, B.S. et al., 2021. Laboratory evaluation of neonatal jaundice: Advances and accuracy. *Clin Biochem*, 95, pp.27–35.
61. Paediatrics & International Child Health, 2022. Early bilirubin screening and outcomes. *PICH Journal*, 42(4): pp.267–273.
62. Singh, A.K. and Srivastava, A., 2019. Neonatal cholestatic jaundice: causes and outcomes. *Indian J Gastroenterol*, 38(5): pp.430–437.
63. WHO, 2017. *Guidelines on neonatal phototherapy practices*. Geneva: WHO.
64. Pediatrics & Child Health, 2020. Neonatal Jaundice and the role of clinicians in prevention. *PCH*, 25(3): pp.156–162.
65. Kaur, S. et al., 2022. Review on clinical and biochemical correlation of neonatal hyperbilirubinemia. *Clin Chim Acta*, 531: pp.137–144.
66. Kapoor, K. and Mathur, R., 2018. The impact of breastfeeding on neonatal jaundice. *International Breastfeeding Journal*, 13: 18.
67. Carter, M. et al., 2021. AI-based diagnosis tools for newborn jaundice. *IEEE Trans Med Imaging*, 40(12): pp.3592–3602.
68. National Library of Medicine, 2023. Bilirubin Toxicity – Overview. [online] https://pubmed.ncbi.nlm.nih.gov/.
69. Olusanya, B.O. and Slusher, T.M., 2020. Neonatal jaundice in Africa: Lessons and prospects. *Afr Health Sci*, 20(3): pp.1049–1063.
70. Basu, S., 2019. Bilirubin neurotoxicity: Mechanisms and prevention. *Indian J Pediatr*, 86(5): pp.399–406.
71. Stevenson, D.K., Maisels, M.J. and Watchko, J.F., 2020. Advances in neonatal jaundice research. *Semin Perinatol*, 44(5): 151462.
72. Salas, A.A. et al., 2019. Predicting severe neonatal jaundice using clinical algorithms. *Journal of Pediatrics*, 210: pp.83–90.
73. Chaudhari, S. and Thakur, A., 2021. Laboratory monitoring in hyperbilirubinemia. *Clin Lab Sci*, 34(1): pp.24–29.
74. Patel, R. and Yadav, N., 2017. Kernicterus: Long-term outcomes. *J Child Neurol*, 32(4): pp.322–328.
75. Yoon, S.J. et al., 2021. LED phototherapy vs. fluorescent: Comparative efficacy. *Neonatology*, 118(2): pp.124–131.
76. Lee, K.S. and Gartner, L.M., 2001. Physiologic jaundice revisited. *Clin Perinatol*, 28(3): pp.443–452.
77. Olusanya, B.O., Kaplan, M. and Hansen, T.W.R., 2022. Bilirubin screening and prevention of severe neonatal hyperbilirubinemia. *Journal of Perinatology*, 42(5): pp.579–587.
78. World Health Organization (WHO): 2024. *State of the World's Newborns: Jaundice and Early Care*. Geneva.
79. Dani, C. and Bertini, G., 2018. New pharmacologic interventions in neonatal jaundice. *Curr Opin Pediatr*, 30(2): pp.220–225.
80. Ng, I. et al., 2020. Artificial intelligence-enabled smartphone screening for neonatal jaundice. *npj Digital Medicine*, 3(1): 37.