

Standard Treatment Guidelines

Detection, management and prevention of hyperbilirubinemia in term and late preterm newborn infants

Quick Reference Guide
October 2016

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Introduction

Jaundice refers to the yellow discoloration of the skin and the sclera caused by the accumulation of a pigment (bilirubin) in the skin and mucous membranes. It is seen in neonates when the serum bilirubin levels exceed 5-7 mg/dL. Approximately 60% of term and 80% of preterm infants develop jaundice in the first week of life, and about 10% of breastfed infants are still jaundiced at 1 month.

Visible jaundice usually appears between 24 to 72 hours of age. The total serum bilirubin (TSB) level usually rises in term infants by 3 days of age and then falls. In preterm infants, the peak level occurs around 3 to 7 days after birth. It may take weeks before the TSB levels falls under 2 mg/dL in both term and preterm infants. Jaundice is not an indication of an underlying disease for most infants, and this early jaundice (termed 'physiological jaundice') is generally harmless.

Hyperbilirubinemia typically refers to serum bilirubin levels beyond the normal range and is a common problem in neonates. (1)A significant proportion of these neonates develop pathological jaundice (jaundice requiring treatment) during the first week of life (2). It is also one of the leading causes of hospitalization in the first week of life globally (3-5).The overall incidence of hyperbilirubinemia (>15 mg/dL) has been reported as 3.3% in intramural neonates and 22.1%in extramural neonates(2).

Timely and appropriate treatment with phototherapy and/or exchange transfusion is effective in decreasing excessive bilirubin levels. However, failure of instituting appropriate therapy results in acute bilirubin encephalopathy (ABE) which if not treated immediately, might go on to develop kernicterus and other long term neurological deficits including cerebral palsy, sensorineural hearing loss, intellectual difficulties or gross developmental delays (6-10). It is estimated that nearly 5,00,000 term and late preterm neonates globally are affected by severe hyperbilirubinemia annually and around one-fourth of them die and 63,000 survive with neurological disability (11). Three-fourth of these affected infants reside in sub-Saharan Africa and South Asia (12).

The purpose of the guideline

There is a need for a standard guideline for the management of neonatal hyperbilirubinemia in term and late preterm newborn infants in India. The context for the detection, management and prevention of neonatal hyperbilirubinemia in India is different from other countries.

The published evidence based guidelines on early detection, management and prevention of neonatal hyperbilirubinemia by various bodies including American Academy of Pediatrics (13) and National Institute for Health and Clinical Excellence (14) primarily takes care of the need of high income countries. The low and middle-income countries including India are following these guidelines due to dearth of literature and absence of such evidence based guidelines from their own setting.

There is an increased incidence of significant hyperbilirubinemia in India due to various risk factors including racial and genetic factors, widespread practice of exclusive breastfeeding, higher prevalence of G6PD deficiency in some parts of the country, more neonates with low albumin at birth, higher bilirubin levels in summer season due to dehydration, blood group incompatibilities and infections(15, 16). Lack of knowledge among mother and family members about jaundice (17) and poor transport facilities especially in rural areas often results in delay in seeking medical advice. The situation is further compounded by “why worry” attitude among healthcare professionals especially in the dearth of substantial data documenting bilirubin induced neurological dysfunction (BIND) on arrival to health facility(18). Inadequate knowledge among healthcare professionals, limited facilities for clinical investigations, lack of standardised protocol for management (including absence of monitoring serum bilirubin while under phototherapy) and inconsistent functional status of available phototherapy devices, often results in inappropriate treatment thus resulting in BIND(19-22). Even the lack of exchange transfusion facilities at majority of the healthcare setting due to non-availability of blood or expertise results in permanent neurological dysfunction which could be easily avoided by doing early exchange transfusion.

Though the guidelines published by National Neonatology Forum, India (NNF 2010) (22) have tried to provide a practical framework for managing neonatal hyperbilirubinemia in Indian setting, these guidelines are meant for only tertiary care health facilities. In view of the above stated reasons and opening of Special Care Newborn Units (SCNUs) and private health facilities delivering level II neonatal care in a big way; the current guideline has been

developed for the management of neonatal hyperbilirubinemia in late preterm and term infants in the Indian context for health care facilities at all levels.

Approach of the guideline

The guidelines have been commissioned to enable a systematic cost-effective approach for the detection, management and evaluation of neonatal hyperbilirubinemia in late preterm and term infants in India. This guideline and its accompanying implementation tools in the form of a quick reference guide, flow charts, and quality standards will serve as a valuable reference material for healthcare providers, patients and administrators. While formulating these guidelines the main outcome measures taken into consideration have been mortality, incidence of acute bilirubin encephalopathy, incidence of chronic bilirubin encephalopathy, hearing Loss, incidence of exchange transfusion, incidence of severe hyperbilirubinemia, duration of phototherapy and incidence of readmissions required for hyperbilirubinemia

- This guideline has a primary care focus and a public health approach. The focus of the primary care is to improve the early detection and the timely treatment to prevent long term neurological deficits. Increasing awareness among public especially mother and family members at the time of discharge about the need for jaundice evaluation in first week of life in face of early discharges from health facilities in India will improve this dismal situation and result in improving intact survival.
- These guidelines will also facilitate effective advocacy and mobilisation of requisite resources for the optimal care of newborn infants with hyperbilirubinemia at all levels.
- The guideline presented covers detection, management and prevention of hyperbilirubinemia in term and late preterm newborn infants in primary, secondary and tertiary care setting and includes an algorithmic approach (figure 1) to a newborn with or at risk of hyperbilirubinemia.

Full Guideline Title: Detection, management and prevention of hyperbilirubinemia in term and late preterm newborn infants

Population

Groups that will be covered

- a) Neonates \geq 35 weeks

Groups that will not be covered

- a) Preterm neonates < 35 weeks
- b) Neonates with conjugated hyperbilirubinemia

Health Care Setting

- a) Primary care
- b) Secondary and tertiary care

Disease or risk condition

At risk or having jaundice

Key Clinical issues that will be covered in this guideline

I. Screening and Diagnosis

- 1.1 What should be the screening protocol for detection of jaundice in neonates?
- 1.2 Which neonates are at a higher risk of hyperbilirubinaemia?
- 1.3 What is the accuracy of transcutaneous bilirubinometry in recognising neonatal hyperbilirubinaemia and how should it be done?
- 1.4 How will you interpret serum bilirubin levels and manage hyperbilirubinaemia?
- 1.5 What should be optimum discharge and follow-up timing and the assessment policy to minimize the subsequent risk of severe hyperbilirubinemia and acute bilirubin encephalopathy?
- 1.6 What should be included in the formal assessment of a neonate with neonatal hyperbilirubinaemia?
- 1.7 How can we prevent severe hyperbilirubinemia?

II. Treatment of hyperbilirubinemia

- 2.1 Phototherapy
- 2.2 Exchange transfusion
- 2.3 Other modalities
- 2.4 What should be the frequency of long term follow up of neonates with hyperbilirubinemia and what all should be evaluated at follow up?
- 2.5 Information and support which should be given to parents/caregivers of neonates with neonatal hyperbilirubinaemia?

Key recommendations

1. *Screening and assessment*

1.1 What should be the screening protocol for detection of jaundice in neonates? (14,22)

Recommendation

1. Healthcare professionals should all look for jaundice (visual inspection) in babies (Figure 1)
2. Assessment of all newborns for jaundice should be done every 12 hours especially in the initial 3 to 5 days.
3. Monitoring for development of severe neonatal jaundice may be needed till end of first week of postnatal life.

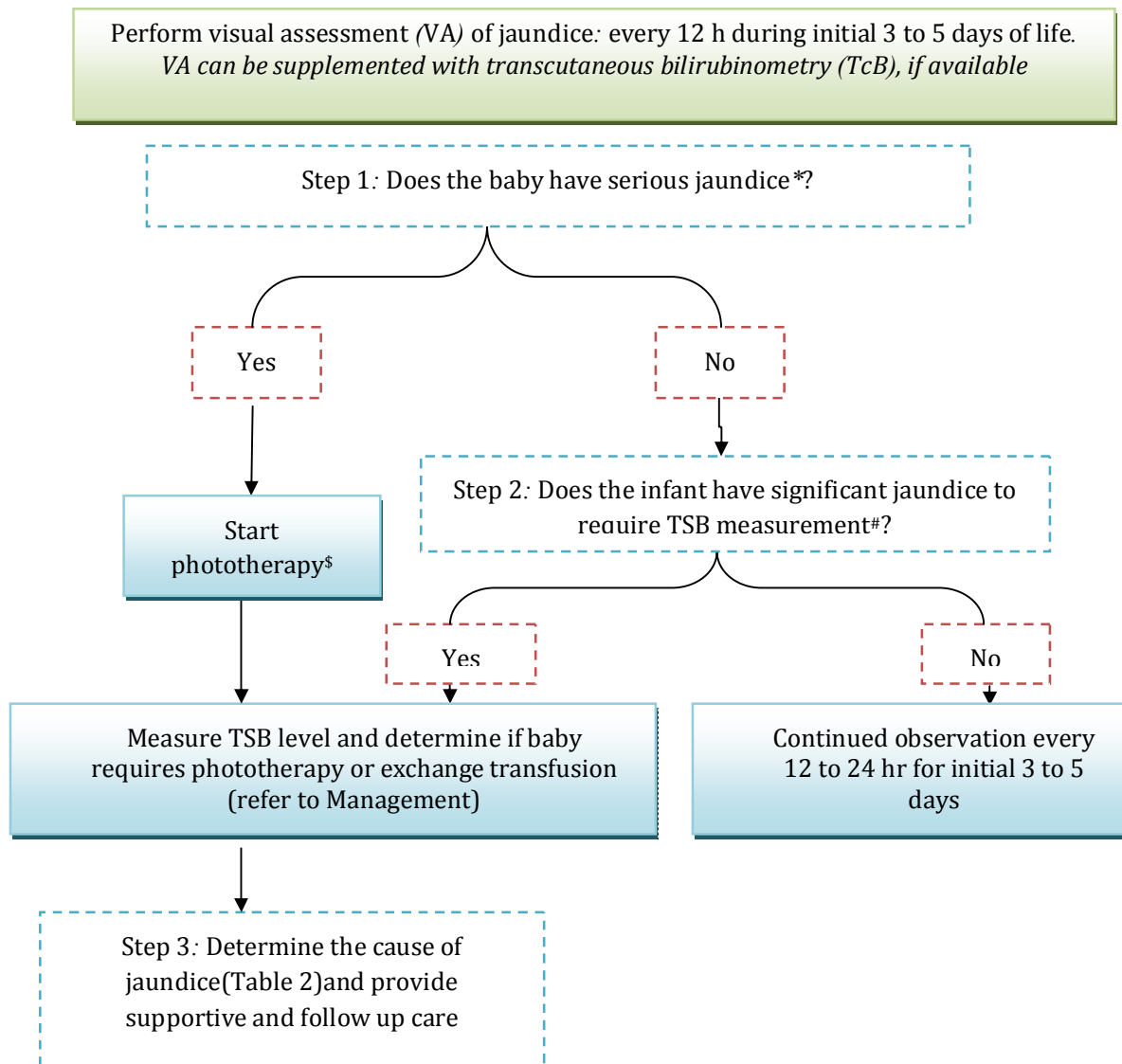
1.2 Which neonates are at a higher risk of hyperbilirubinaemia? (13, 22)

Recommendation

Identify neonates as being more likely to develop significant hyperbilirubinaemia if they have **ANY** of the following factors:

- Gestational age under 38 weeks
- A previous sibling with neonatal hyperbilirubinaemia requiring phototherapy
- Mother's intention to breastfeed exclusively
- Visible jaundice in the first 24 hours of life.
- Visible jaundice at discharge
- Setting of blood group incompatibility
- High prevalence of G6PD deficiency, primipara mother
- Weight loss at discharge >3% per 24 h of age or >7% cumulative weight loss

Figure 1: Approach to an infant with jaundice



***Serious jaundice (Any one of following):**

- a. Presence of visible jaundice in first 24 h
- b. Yellow palms and soles anytime
- c. Signs of acute bilirubin encephalopathy or kernicterus: hypertonia, abnormal posturing such as arching, retrocollis, opisthotonus or convulsion, fever, high pitched cry)
- d. IF AVAILABLE: Serum bilirubin or TcB value more than 95th centile as per age specific nomogram(23)

#Measure serum bilirubin if:

- a. Jaundice in first 24 hour
- b. Beyond 24 hr: if on visual assessment or by transcutaneous bilirubinometry, TSB is likely to be more than 12 to 14 mg/dL or approaching phototherapy range or beyond.
- c. If you are unsure about visual assessment

§Though it is important to start immediate phototherapy, it is also important to document serum bilirubin simultaneously.

1.3 What is the accuracy of transcutaneous bilirubinometry in recognising neonatal hyperbilirubinaemia and how should it be done?

1.3.1 Clinical examination for jaundice

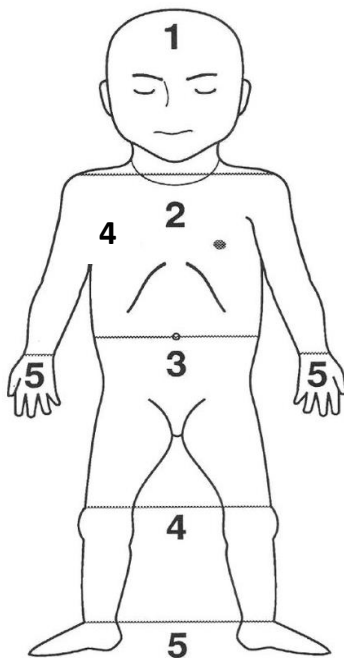
Essential steps for screening and assessment of jaundice*

1. Examine the baby in bright natural light. Alternatively, the baby can be examined in white fluorescent light. Make sure there is no yellow/ off white background.
2. Make sure the baby is naked.
3. Examine blanched skin and gums or sclerae
4. *Depth of jaundice (degree of yellowness) should be carefully noted as it is an important indicator of level of jaundice and it does not figure out in Kramer's rule) (figure 2)*

A deep yellow staining (even in absence of yellow soles or palms) is often associated with sever jaundice and therefore TSB should be estimated in such circumstances.

*Important notes

- 1 Visual inspection of jaundice 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 particularly when TSB is less than 12 to 14 mg/dL
- 2 Absence of jaundice on visual inspection reliably excludes the jaundice.
- 3 All newborns with visible jaundice should be evaluated with TcB or TSB
- 4 If transcutaneous bilirubinometer is available, use it in babies with a gestational age of 35 weeks or more and postnatal age of more than 24 hours and if it indicates a bilirubin level greater 14 mg/dL, check serum bilirubin.



1. Face	5-7 mg/dL
2. Chest	8-10 mg/dL
3. Lower abdomen/thigh	12 to 15 mg/dL
4. Arms/ lower legs	15 to 18 mg/dL
5. Soles/Palms	>15 mg/dL

Figure 2: The extent of jaundice (Kramer's rule)(24)

1.3.2 Transcutaneous and total serum bilirubin

Measurement of bilirubin

Transcutaneous bilirubinometry (TcB)

1. TcB is a useful adjunct to TSB measurement, and routine employment of TcB can reduce need for blood sampling by nearly 30%.
2. Current devices are costly and have a significant recurring cost of consumables such as disposable tips etc.
3. TcB can be used in infants of 35 weeks or more of gestation after 24 hr.
4. TcB becomes unreliable once TSB level goes beyond 14 mg/dL.
5. Hour specific TcB can be used for prediction of subsequent hyperbilirubinemia. TcB value below 50th centile for age would rule out the risk of subsequent hyperbilirubinemia with high probability (high negative predictive value)(23)
6. Trends in TcB values by measuring 12 hr apart would have a better predictive value than a single value.

Measurement of TSB

- a. Indication of TSB measurement:
 - i. Jaundice in first 24 hour
 - ii. Beyond 24 hr: if visually assessed jaundice is likely to be more than 14 mg/dL *or* approaching the phototherapy range *or* beyond.
 - iii. If you are unsure about visual assessment
 - iv. During phototherapy, for monitoring progress and after phototherapy to check for rebound in select cases (such as those with hemolytic jaundice)
- b. Frequency of TSB measurement depends upon the underlying cause (hemolytic versus non-hemolytic) and severity of jaundice as well as host factors such as age and gestation. In general, in non-hemolytic jaundice in term babies, TSB can be performed every 12 hr depending upon age of the baby. As opposed to this, a baby with Rh isoimmunisation would require TSB measurement every 6 to 8 hours during initial 24 to 48 hours or so.
- c. Methods of TSB measurements
 - i. Biochemical: High performance liquid chromatography (HPLC) remains the gold standard for estimation of TSB. However, this test is not universally available and laboratory estimation of TSB is usually performed by Vanden Bergh reaction. It has marked inter laboratory variability with coefficient of variation being up to 10 to 12 percent for TSB and over 20 percent for conjugated fraction. (25)
 - ii. Micro method for TSB estimation: It is based on spectrophotometry and estimates TSB on a micro blood sample. It is useful in neonates, as bilirubin is predominantly unconjugated and can be done bedside.

1.4 How will you interpret serum bilirubin levels and manage hyperbilirubinaemia?

Recommendation

Interpret serum bilirubin levels according to the baby's postnatal age in hours and manage hyperbilirubinaemia as per the guidelines.

1. American Academy of Paediatrics (AAP) criteria should be used for making decision regarding phototherapy or exchange transfusion in these infants. AAP provides two age-specific nomograms- one each for phototherapy and exchange transfusion. The nomograms have lines for three different risk categories of neonates (Figure 2 and 3). These lines include one each for lower risk babies (38 wk or more and no risk factors), medium risk babies (38 wk or more with risk factors, or 35 wk to 37 wk and without any risk factors) and higher risk (35 wk to 37 wk and with risk factors).
2. TSB value is taken for decision making and direct fraction should **NOT** be reduced from it. The babies at lower and higher risk have their cut-offs at approximately 2 mg/dL higher or 2 mg/dL lower than that for medium risk babies, respectively.
3. Risk factors include presence of isoimmune hemolytic anemia, G6PD deficiency, asphyxia, temperature instability, hypothermia, sepsis, significant lethargy, acidosis and hypoalbuminemia.*

*Routine estimation of serum albumin is not recommended

Figure 3: Guidelines for phototherapy in hospitalized infants of 35 or more weeks gestation.

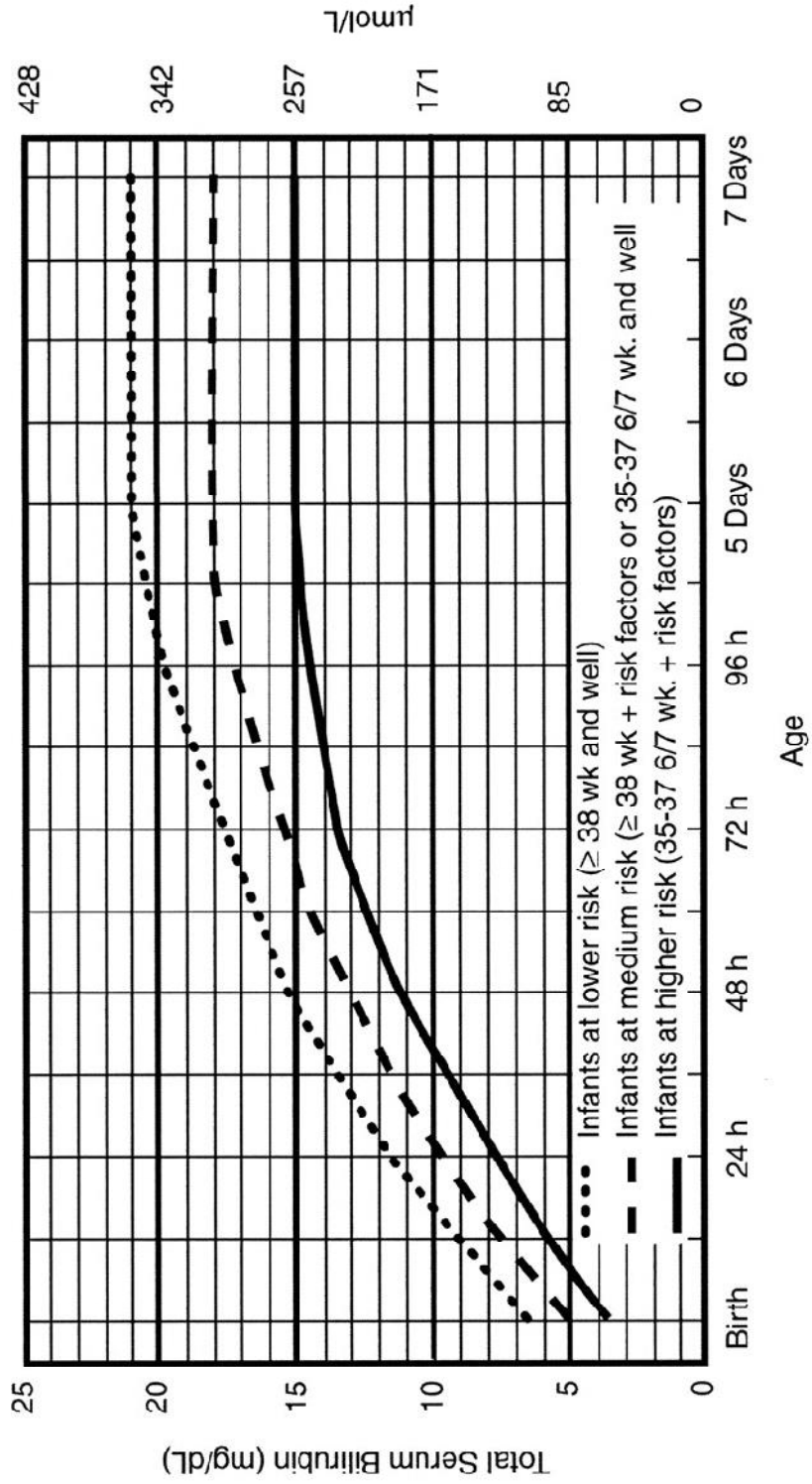
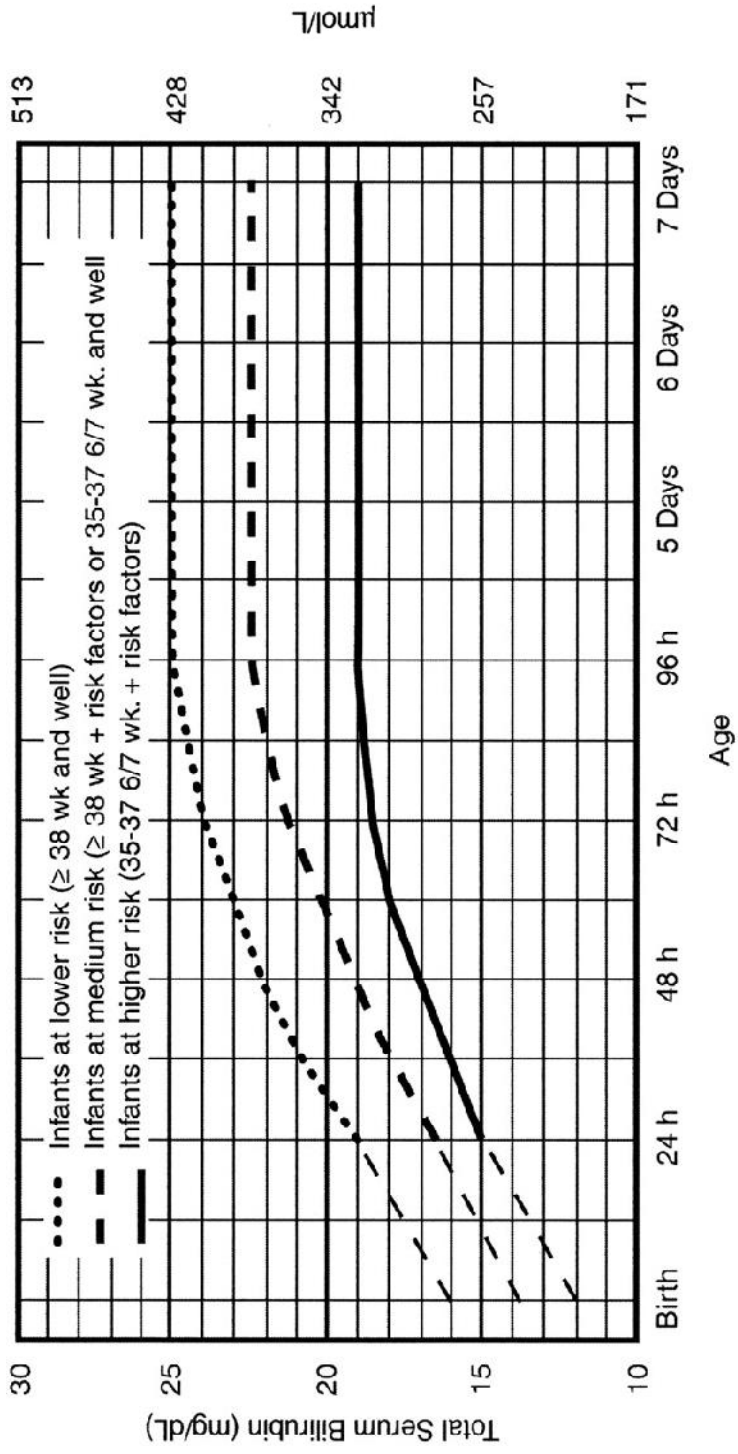


Figure 4 : Guidelines for exchange transfusion in hospitalized infants of 35 or more week's gestation.



1.5 What should be optimum discharge and follow-up timing and the assessment policy to minimize the subsequent risk of severe hyperbilirubinemia and acute bilirubin encephalopathy? (22)

In India, healthy neonates are usually discharged after 24-48 h of normal delivery. In some facilities with high obstetric case load or absence of adequate manpower neonates are discharged even before completing first 24 h of age. Discharge after delivery by cesarean section is more variable with length of stay varying from 3 to 7 days. Due to continuing rise of bilirubin and absence of supervision for ensuring optimal feeding, neonates discharged home before completing 48-72 h of age are at high risk of developing undetected pathological hyperbilirubinemia. In India, this risk may be further aggravated due to absence of any formal system of follow-up home-visits by health care personnel (e.g. public health nurse) and due to traditional practice of confinement of mother-baby dyad at home for first few weeks after delivery. Neonates delivered at home are also at high risk of undetected pathological hyperbilirubinemia due to same reasons.

The strategy of follow up of all neonates although desirable, is not feasible due to relative shortage of health care personnel and inability of some families to return for follow-up. Therefore follow-up plan may be devised based on pre-discharge risk assessment (Table 1).

Table 1: Suggested follow-up policy (13)

Scenario	Age at discharge	Follow-up
None of risk factors* present	24-72 h	48 h after discharge
	>72 h	Follow-up optional
Any risk factor* present	24-48 h	24 h after discharge
	After 48 hours	48 h after discharge

*History of jaundice needing treatment in previous sibling, setting of blood group incompatibility, visible jaundice at discharge, gestation <38 completed weeks, high prevalence of G6PD deficiency, primipara mother, weight loss at discharge >3% per 24 h of age or >7% cumulative weight loss,

**may need a repeat visit dependina on physician's assessment

1.6 What should be included in the formal assessment of a neonate with neonatal hyperbilirubinaemia? (14)

Recommendation

All neonates should undergo a complete clinical examination including evaluation of intensity of jaundice (24), breast feeding adequacy[#], pallor, splenomegaly, cephalhematoma or other signs of birth trauma, and evaluation for lethargy, poor feeding, general activity and tone.

1. All pregnant women should be tested for ABO and Rh (D) blood types. (14)
2. If a mother has not had prenatal blood grouping or is Rh-negative, a direct antibody test (or Coombs' test), blood type, and an Rh (D) type on the infant's (cord) blood are strongly recommended. (14)
3. **DO NOT** use the albumin/bilirubin ratio when making decisions about the management of hyperbilirubinaemia (14)
4. Do not subtract conjugated bilirubin from total serum bilirubin when making decisions about the management of hyperbilirubinaemia. (14)
5. In addition to a full clinical examination by a suitably trained healthcare professional, **carry out the following tests in babies with hyperbilirubinaemia** (Table 2) as part of an assessment for underlying disease and treatment threshold graphs.

Table 2: Tests to be done in babies with hyperbilirubinaemia

Indications	Assessments
Infant receiving phototherapy	Measure TSB; blood type and DCT (if mother is 'O' or Rh negative); G6PD status; peripheral smear and reticulocyte count
Jaundice present beyond 3 weeks of age*	Total and direct (or conjugated) bilirubin level, thyroid profile (T3, T4, TSH), urine for reducing substances (galactosemia), urine r/m, urine c/s

Important Note*

- Exclude cephalohematoma on examination
- Exclude Rh isoimmunisation
- Excessive weight loss (more than 10%)
- Breast feeding jaundice due to inadequate breast feeding is common
- Presence of direct hyperbilirubinemia (direct bilirubin more than 2 mg/dL at any age) requires specific investigations and care which is beyond the scope of this guideline

[#]Breast feeding is considered adequate if infant passes urine 6 to 8 times in 24 hours, sleeps for 2 to 3 hours after feeds and gains weight adequately after initial 7 to 10 days.

1.7 How can we prevent severe hyperbilirubinemia?(13, 14)

Recommendation

1. All women should be encouraged to breastfeed 8 to 12 times a day
2. Supplementation is recommended only for dehydrated newborns and where weight loss from birth is >10%. Expressed breastmilk is the preferred supplementation.
3. Routine supplementation with intravenous fluids, honey or dextrose water for newborns with jaundice is not recommended
4. No interruption of breastfeeding should be done for any jaundice.

- *Management and treatment*

Therapeutic options in management of hyperbilirubinemia

2.1 Phototherapy for the management of hyperbilirubinemia (14)*

- “ Phototherapy can be delivered by light - emitting diode (LED) or fibreoptic or fluorescent lamps or tubes or bulbs.[#]
- “ Do not use sunlight as treatment for hyperbilirubinaemia. Exposing the baby to sunlight does not help in treatment of jaundice and is associated with risk of sunburn and therefore should be avoided.

*Rash, overheating, dehydration and diarrhoea are the most common side effects of phototherapy. It has photo oxidative effects and hence the parenteral nutrition fluid and some drugs need to be adequately covered during phototherapy

[#]See Appendix A for different phototherapy equipment available in Indian Market

Starting phototherapy

- “ Use serum bilirubin levels **ONLY** for decision making for starting phototherapy
- “ Intensive phototherapy must be ensured for neonates nearing exchange transfusion threshold. Phototherapy can be intensified by adding another light source or increasing the irradiance of the initial light source used.
- “ Increase the area of exposure to light by using double surface phototherapy for severe jaundice.*
- “ It is not necessary to measure spectral irradiance before each use of phototherapy; however it is important to perform periodic checks of phototherapy units to make sure that an adequate irradiance is being delivered.
- “ Phototherapy thresholds presented on seventh day may be used for rest of the neonatal period.

*Severe jaundice defined earlier

Stopping phototherapy

- “ There is no standard for discontinuing phototherapy. For infants who are readmitted after their birth hospitalization (usually for TSB levels of 18 mg/dL or higher), phototherapy may be discontinued when the serum bilirubin level falls below 13 to 14 mg/dL.

Discharge and follow up after phototherapy

- “ If phototherapy is used for infants with hemolytic diseases or is initiated early and discontinued before the infant is 3 to 4 days old, a follow-up bilirubin measurement within 24 hours after discharge is recommended.
- “ For infants who are readmitted with hyperbilirubinemia and then discharged, significant rebound is rare, but a repeat TSB measurement or clinical follow-up 24 hours after discharge is a clinical option.
- “ Checking serum bilirubin 24 h after discharge to check for rebound is optional

Tips for delivering safe and effective phototherapy

- Protect the eyes with eye patches/covers
- Keep the baby naked with a small nappy to cover the genitalia
- Place the baby as close to the lights as the manufacturers' instructions allow.
- Routine position change while the baby is under phototherapy is not recommended.
- Phototherapy does not have to be continuous and can be interrupted for feeding, clinical procedures, and to allow maternal bonding.#
- Using white cloth or aluminum foil around the light source to reflect light back onto the baby, making sure not to impede the airflow that cools the bulbs is optional
- Do not place anything over the top of the phototherapy unit. This may block air vents or light and items may fall on the baby
- Encourage frequent breastfeeding. Unless there is evidence of dehydration, supplementing breastfeeding or providing IV fluids is unnecessary
- Giving frequent feeding will prevent excessive weight loss and temperature from rising
- Visual assessment of jaundice during phototherapy is unreliable
- Ensure all phototherapy equipment is maintained and used according to the manufacturers' guidelines.

#Important note

- ~ The guideline notes that there is no evidence to support the safe use of intermittent phototherapy at moderate or high levels of serum bilirubin (mild hyperbilirubinemia defined as a total bilirubin level of up to 12 mg/dL and high defined as levels above 20 mg/dL in full-term infants. Bilirubin levels between these values indicated moderate hyperbilirubinemia)
- ~ Change tube lights every 6 months (or usage time >1200 hrs) whichever is earlier; or if tube ends blacken or if tubes flicker. Life of Compact Fluorescent lamps is 3000 hours while that of LED bulbs is 30,000 to 50,000 hours.

Failure of phototherapy (22)

- ~ For those infants in the exchange or pre-exchange bilirubin zone, failure of phototherapy has been defined as an inability to observe a decline in bilirubin of 1-2 mg/dL after 4-6 hours and/or to keep the bilirubin below the exchange transfusion level.
- ~ Exchange transfusion is recommended if the TSB rises to these levels despite intensive phototherapy.
- ~ For readmitted infants, if the TSB level is above the exchange level, repeat TSB measurement every 2 to 3 hours and consider exchange if the TSB remains above the levels indicated after intensive phototherapy for 6 hours. However, an exchange transfusion (ET) should be performed at the slightest suspicion of bilirubin encephalopathy irrespective of the bilirubin value.

2.2 Exchange transfusion for management of hyperbilirubinemia (14)

- Exchange transfusion should be done by central or peripheral route aiming replacement of double the baby's blood volume and by skilled personnel in a well-equipped centre.
- Immediate EBT is recommended if infant shows signs of ABE or if TSB is ≥ 25 mg/dL above the recommended age and risk specific cut off TSB
- For Rhesus isoimmunization, the best choice would be O (Rh) negative packed cells suspended in AB plasma. O (Rh) negative whole blood or cross-matched baby's blood group (Rh negative) may also be used.
- For ABO isoimmunization, O group (Rh compatible) packed cells suspended in AB plasma or O group whole blood (Rh compatible with baby) should be used.
- In other situations baby's blood group should be used. All blood must be cross matched against maternal plasma.
- Blood volume used: $2 \times (80-100 \text{ ml/kg}) \times \text{birth weight in kg}$.

2.3 Other modalities for management of hyperbilirubinemia (14)

- No role of phenobarbitone, tin mesoporphyrin, Agar, Albumin, charcoal, cholestyramine, clofibrate, glycerine, chinese herbs, homeopathy, acupuncture, riboflavin or manna in management of hyperbilirubinemia
- Routine use of Intravenous immunoglobulin (IVIg) for Rhhaemolytic disease of newborn and ABO disease is not recommended as evidence from studies with low risk of bias indicates no benefit in Rhhaemolytic disease of newborn and studies suggesting benefit in ABO incompatibility had a high risk of bias. (26)

2.4 What should be the frequency of long term follow up of neonates with hyperbilirubinemia and what all should be evaluated at follow up?

- When infants with hyperbilirubinemia are identified and treated appropriately, the outcome is excellent with minimal or no additional risk for adverse neurodevelopmental sequelae.
- Neonates with hyperbilirubinemia requiring exchange transfusion require:
 - Follow up (at 3 months and 18 months postnatal age) for formal development assessment
 - Hearing evaluation of these neonates by brain stem evoked response audiometry (prior to 3 months)
- Subsequent follow up of these neonates is 6 monthly (or more frequently (if the developmental assessment mandates the same
- Other follow up (for vaccination, growth and feeding can continue as for a normal neonate)

2.4 What information and support should be given to parents/care givers of babies with neonatal hyperbilirubinaemia?

Offer parents or care givers information about neonatal jaundice but should be tailored to their needs and expressed concerns. This information should be provided through verbal discussion backed up by written information whenever possible. (14)

Care should be taken to avoid causing unnecessary anxiety to parents or care-givers.

Information should include:

- “ factors that influence the development of significant hyperbilirubinaemia
- “ how to check the baby for jaundice
- “ what to do if they suspect jaundice
- “ the importance of recognising jaundice in the first 24 hours and of seeking urgent medical advice
- “ the importance of checking the baby’s nappies for dark urine or pale chalky stools
- “ the fact that neonatal jaundice is common, and reassurance that it is usually transient and harmless when treated appropriately
- “ reassurance that breastfeeding should continue

Information about treatment including phototherapy

- “ anticipated duration of treatment
- “ reassurance that breastfeeding, nappy-changing and cuddles can usually continue.
- “ Encourage mothers of with jaundice to breastfeed frequently, and to wake the baby for feeds if necessary.
- “ Provide lactation/feeding support to mothers whose baby is visibly jaundiced.
- “ why phototherapy is being considered
- “ why phototherapy may be needed to treat significant hyperbilirubinaemia
- “ the possible adverse effects of phototherapy
- “ the need for eye protection and routine eye care
- “ reassurance that short breaks for feeding, nappy changing and cuddles will not alter course of jaundice and efficacy of phototherapy
- “ what might happen if phototherapy fails
- “ rebound jaundice
- “ potential long-term adverse effects of phototherapy

Information on exchange transfusion

- “ Offer parents or care givers information on exchange transfusion including:
- “ the baby be admitted to an intensive care bed
- “ why an exchange transfusion is being considered
- “ the possible adverse effects of exchange transfusions
- “ when it will be possible for parents or care givers to see and hold the baby after the exchange transfusion.
- “ when it will be possible for parents or carers to see and hold the baby after the exchange transfusion.

References:

1. Ip S, Chung M, Kulig J, et al. An evidence-based review of important issues concerning neonatal hyperbilirubinemia. *Pediatrics* 2004;114:e130-53
2. Report 2002-2003: National Neonatal Perinatal Database Network. New Delhi: National Neonatology Forum of India; 2004.
3. The Young Infants Clinical Signs Study Group. Clinical signs that predict severe illness in children under age 2 months: a multicentre study. *Lancet*. 2008;371:135–42.
4. Burke BL, Robbins JM, Bird TM, Hobbs CA, Nesmith C, Tilford JM. Trends in hospitalizations for neonatal jaundice and kernicterus in the United States, 1988–2005. *Pediatrics*. 2009;123:524–32.
5. Tomashek KM, Crouse CJ, Iyasu S, Johnson CH, Flowers LM. A comparison of morbidity rates attributable to conditions originating in the perinatal period among newborns discharged from United States hospitals, 1989–90 and 1999–2000. *Paediatr Perinat Epidemiol*. 2006;20:24–34.
6. Mwaniki MK, Atieno M, Lawn JE, Newton CR. Long-term neurodevelopmental outcomes after intrauterine and neonatal insults: a systematic review. *Lancet*. 2012;379:445–52.
7. Gladstone M. A review of the incidence and prevalence, types and aetiology of childhood cerebral palsy in resource-poor settings. *Ann Trop Paediatr*. 2010;30:181–96.
8. Amin SB, Smith T, Wang H. Is neonatal jaundice associated with autism spectrum disorders: a systematic review. *J Autism Dev Disord*. 2011;41:1455–63.
9. Olusanya BO, Somefun AO. Sensorineural hearing loss in infants with neonatal jaundice in Lagos: a community-based study. *Ann Trop Paediatr*. 2009;29:119–28.
10. Maulik PK, Darmstadt GL. Childhood disability in low- and middle-income countries: overview of screening, prevention, services, legislation, and epidemiology. *Pediatrics*. 2007;120Suppl 1:S1–55.
11. Olusanya BO, Ogunlesi TA, Kumar P, Boo NY, Iskander IF, Almeida DF, Vaucher YE, and Slusher TM. Management of late-preterm and term infants with hyperbilirubinaemia in resource-constrained settings. *BMC Pediatr*. 2015; 15: 39.
12. Bhutani VK, Zipursky A, Blencowe H, Khanna R, Sgro M, Ebbesen F, et al. Neonatal hyperbilirubinemia and Rhesus disease of the newborn: incidence and impairment estimates for 2010 at regional and global levels. *Pediatr Res*. 2013;74Suppl 1:86–100.
13. American Academy of Pediatrics Subcommittee on Hyperbilirubinemia. Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. *Pediatrics*. 2004 Jul;114(1):297-316.
14. Neonatal Jaundice 2010 Available at <https://www.nice.org.uk/guidance/cg98/evidence/full-guideline-245411821>. Accessed on 18 May, 2016
15. Narang A, Gathwala G, Kumar P. Neonatal jaundice: an analysis of 551 cases. *Indian Pediatr* 1997;34:429-32.
16. Olusanya BO, Ogunlesi TA, Slusher TM. Why is kernicterus still a major cause of death and disability in low and middle-income countries? *Arch Dis Child*. 2014;99:1117–21.

17. Bhutani VK, Johnson LH. Managing the assessment of neonatal jaundice: importance of timing. *Indian J Pediatr.* 2000 Oct;67(10):733-7.
18. Bhutani VK, Cline BK, Donaldson KM, Vreman HJ. The need to implement effective phototherapy in resource-constrained settings. *Semin Perinatol.* 2011;35:192–7.
19. Cline BK, Vreman HJ, Faber K, Lou H, Donaldson KM, Amuabunosi E, et al. Phototherapy device effectiveness in Nigeria: irradiance assessment and potential for improvement. *J Trop Pediatr.* 2013;59:321–5.
20. Pejaver RK, Vishwanath J. An audit of phototherapy units. *Indian J Pediatr.* 2000;67:883–4.
21. Owa JA, Ogunlesi TA. Why we are still doing so many exchange blood transfusion for neonatal jaundice in Nigeria. *World J Pediatr.* 2009;5:51–5.
22. NNF 2010. Available at http://aimaonline.org/iap-neochap-2013/uploads/acd-corner/nnf_guidelines-2011.pdf. Accessed on 18th May, 2016
23. Bhutani VK, Stark AR, Lazzaroni LC, Poland R, Gourley GR, Kazmierczak S, Meloy L, Burgos AE, Hall JY, Stevenson DK; Initial Clinical Testing Evaluation and Risk Assessment for Universal Screening for Hyperbilirubinemia Study Group. Predischarge screening for severe neonatal hyperbilirubinemia identifies infants who need phototherapy. *J Pediatr.* 2013 Mar;162 (3):477-482
24. Kramer LI. Advancement of dermal icterus in jaundiced newborn. *Am J Dis Child* 1969;118:454-8.
25. van Imhoff DE, Dijk PH, Weykamp CW, Cobbaert CM, Hulzebos CV; BARTrial Study Group. Measurements of neonatal bilirubin and albumin concentrations: a need for improvement and quality control. *Eur J Pediatr* 2011;170:977-82.
26. Louis D, More K, Oberoi S, Shah PS. Intravenous immunoglobulin in isoimmune haemolytic disease of newborn: an updated systematic review and meta-analysis. *Arch Dis Child Fetal Neonatal Ed.* 2014 Jul;99(4):F325-31. Epub 2014 Feb 10.

Appendix A

Phototherapy units available in the market

S.No.	Type of unit	Principals	Dealer	Unit cost (Rs.)
A.	White fluorescent tube (6 to 8; 20w)	*	*	20,000
	Double surface Fluorescent			35,000
B.	Compact fluorescent lights (6 to 8; 21w)	Medela	Rohit Surgials	60,000
		Phoenix	Phoenix	25,000
		Nice Neotech	SBP Mediare	20,000
		SS Technomed	Global Medical Sys	20,000
		Meditrin	Meditrin	25,000
C.*	Blue light (2 to 4; 20w) and white (2 to 4; 20w)	Atom	Vishal Surgical	40,000-2,00,000
		Medela	Rohit Surgical	
		Drager	Drager	
		Wyer	Rustagi Surgical	
		Ameda	Medisphere	
		Heraeus	Medex	
		Choongwae	Global Medical	
		Phoenix	Phoenix	
D.	Halogen bulb (Single; 150w; 21v)	Datex-Ohmeda	Phoenix	60,000-90,000
		Olympic	Rustagi Surgical	
		Hillrom	Phoenix	
E.	Bili-Blanket Fibreoptic Bili Bed™	Ginevri	Global Med	1,00,000-2,50,000
		Wallaby	System	
		Medela	Global Med.	
		Olympic	System	
		Datex-	Rohit Surgical	
		Ohmeda	Rohit Surgical	
		Ibis medical	Ibis medical	

	Principals	Dealer	
• LED	Shrichitra	Shrichitra	40,000
• Lullaby LED	GE	GE	60,000
• LED high intensity spot (Bilitron 3006/ Bilitron bed 5006/ Bilitron sky 5006)	Fanem	Fanem	80,000
• LED high intensity spot	Phoenix	Phoenix	40,000
• Sunshine LED	SS technomed		40,000
• Ibis medical	Ibis Medical		50,000