Can Severe Hyperbilirubinemia be Accurately Predicted?

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Kernicterus is a rare but devastating sequel of extreme hyperbilirubinemia. If we can prevent extreme hyperbilirubinemia, we should be able to prevent almost all cases of kernicterus, but jaundice is very common and extreme hyperbilirubinemia (≥30 mg/dL) is rare. With increasing emphasis on initiation of breast feeding soon after birth and thereafter early discharge of healthy babies, so to make sure that we do not miss these rare infants, we need to follow many newborns and treat some with phototherapy who will never develop severe hyperbilirubinemia.

An hour-specific TSB before hospital discharge can predict which newborn is at high, intermediate or low risk for developing clinically significant hyperbilirubinemia (specifically defined as TSB levels >/=95th percentile for age in hours). Risk designation and subsequent increases or decreases of in TSB can be easily monitored on an hour-specific percentile based predictive bilirubin nomogram (Bhutani's chart Fig.1). This would facilitate targeted intervention and follow-up in a safe, cost-effective manner. In conjunction with bilirubin practice parameter of the American Academy of Pediatrics, it would reduce the potential risk for bilirubin-induced neurologic dysfunction.

Timed TSB / TcB Measurements:

- Carefully timed TSB / TcB measurements can be used to predict the chances of developing severe hyperbilirubinemia.
- Timed measurement of TSB / TcB concentration at discharge (between 18 h and three days of age) in appropriate for gestation age late preterm and term neonates, who do not have positive direct Coomb test, can predict a later TSB measurement greater than the 95th percentile within stated confidence limits (the 95th percentile was approximately 300 μmol/L after 96 h of age)
- TSB / TcB concentration below the 40th percentile at the time of measurement, less likely to develop TSB concentration greater than the 95th percentile.

- The TSB / TcB concentration between the 40th and the 75th percentiles, only 2.2% of infants can develop TSB concentration greater than the 95th percentile.
- Infants with TSB / TcB concentration above the 75th percentile, 12.9% can subsequently have exceeding the 95th percentile.
- The best available method for predicting severe hyperbilirubinemia appears to be the use of a timed TSB / TcB measurement analyzed in the context of the infant's gestational age.
- Infants of less than 38 weeks' gestation whose TSB / TcB concentration is greater than the 75th percentile have a greater than 10% risk of developing severe hyperbilirubinemia; similarly, infants of 39 to 40 weeks' gestation whose TSB / TcB concentration is above the 95th percentile have a greater than 10% risk

Umbilical cord blood TSB

- Poor positive predictive value (4.8%).
- But please mention levels above which it will be considered abnormal

Universal haemoglobin assessment:

- Routine umbilical cord blood hemoglobin or hematocrit measurement does not aid in the prediction of severe hyperbilirubinemia

Blood group and Coomb's testing:

- It is reasonable to perform a Direct Antiglobulin Test (DAT) in clinically jaundiced infants of mothers who are group O and in infants with an elevated risk of needing therapy (ie, in the high-intermediate zone).
- The results will determine whether they are low risk or high risk, and may therefore affect the threshold at which therapy would be indicated
- The usual antenatal screen for a panel of red cell antibodies occasionally identifies additional mothers who will deliver infants at increased risk of hemolysis. The significance of the various antibodies differs; in such infants, analysis of blood group and a

DAT is usually required, closer follow-up and earlier therapy may be needed, and a consultation with a paediatric hematologist or neonatologist is suggested.

G6PD deficiency:

- Newborns with glucose-6-phosphate dehydrogenase (G6PD) deficiency have an increased incidence of severe hyperbilirubinemia (evidence level 1b). Testing for G6PD deficiency in babies whose ethnic group or family history suggest an increased risk of G6PD deficiency is advised (eg, Mediterranean , Middle Eastern, African or South-east Asian origin).
- Testing of both girls and boys who are at risk is advised
- A test for G6PD deficiency should be considered in all infants with severe hyperbilirubinemia (evidence level 5).

End Tidal CO monitoring:

- Exhaled carbon monoxide is increased during hemolysis.
- Prediction of severe hyperbilirubinemia is not improved by measuring the end-tidal carbon monoxide concentration, in addition to a timed TSB measurement (evidence level 1b).

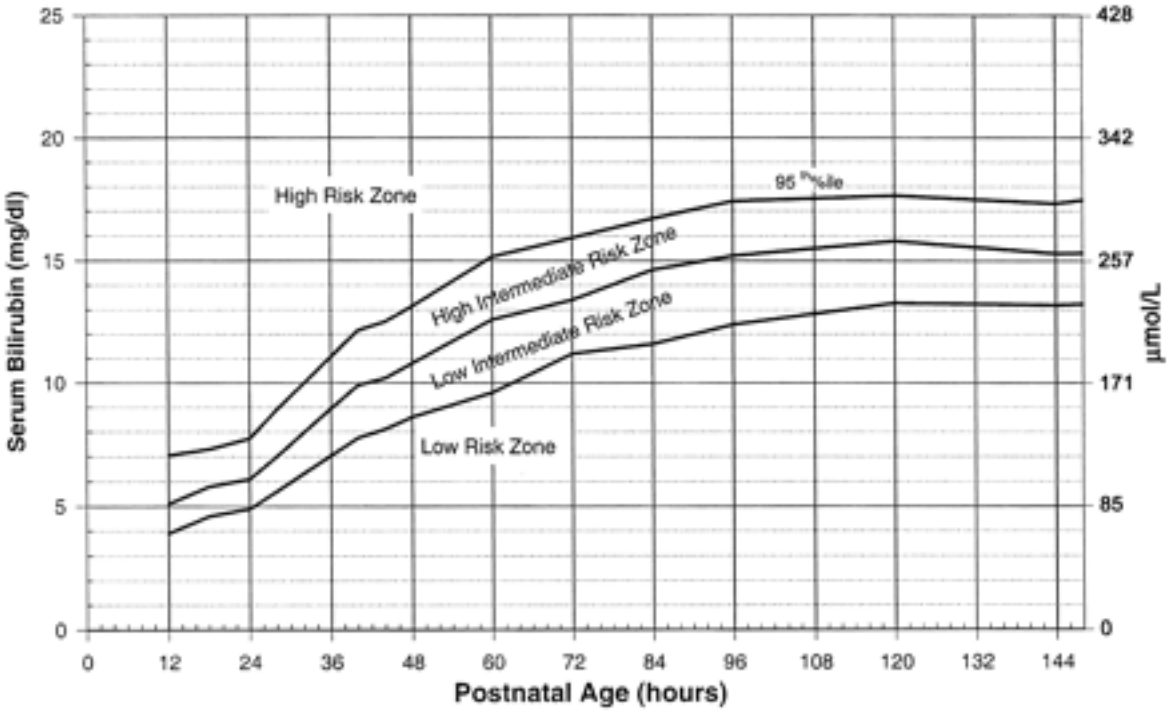
Recommendation:

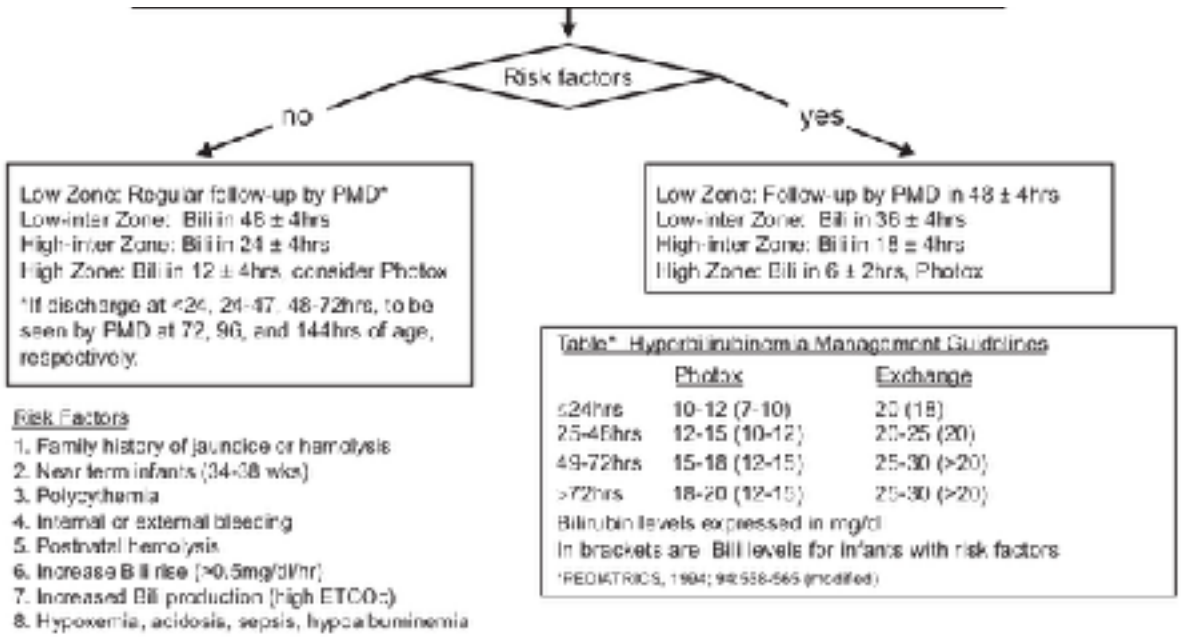
- Carefully timed TSB measurements can be used to predict the chances of developing severe hyperbilirubinemia.
- All babies being discharged from hospital before 72 hours age must be followed up within 48 hours and earlier if indicated by Bhutani chart
- All mothers should be tested for ABO and Rh(D) blood types and be screened for red cell antibodies during pregnancy (recommendation grade D

- If the mother was not tested, cord blood from the infant should be sent for evaluation of the blood group and a DAT (Coombs test) (recommendation grade D).
- Blood group evaluation and a DAT should be performed in infants with early jaundice of mothers of blood group O (recommendation grade B).
- A test for G6PD deficiency should be considered in all infants with severe hyper-bilirubinemia (recommendation grade D).

Reference:

KJ Barrington, K Sankaran; Canadian Paediatric Society, Fetus and Newborn Committee 2018.


Serum Bilirubin (mg/dl)
µmol/L
Postnatal Age (hours)
High Risk Zone
High Intermediate Risk Zone
Low Intermediate Risk Zone
Low Risk Zone
95 %ile
25
20
15
10
5
0
428
342
257
171
85
0
0
12
24
36
48
60
72
84
96
108
120
132
144


Risk factors
no
yes
Low Zone: Regular follow-up by PMD*
Low-inter Zone: Bili in 48 ± 4hrs
High-inter Zone: Bili in 24 ± 4hrs
High Zone: Bili in 12 ± 4hrs, consider Phototx
*If discharge at <24, 24-47, 48-72hrs, to be seen by PMD at 72, 96, and 144hrs of age, respectively.
Low Zone: Follow-up by PMD in 48 ± 4hrs
Low-inter Zone: Bili in 36 ± 4hrs
High-inter Zone: Bili in 18 ± 4hrs
High Zone: Bili in 6 ± 2hrs, Phototx
Risk Factors
1. Family history of jaundice or hemolysis
2. Near term infants (34-36 wks)
3. Polycythemia
4. Internal or external bleeding
5. Postnatal hemolysis
6. Increase B li rise (>0.5mg/dl/hr)
7. Increased Bil production (high ETCO:)
8. Hypoxemia, acidosis, sepsis, hypoalbuminemia
Table* Hyperbilirubinemia Management Guidelines
Phototx
Exchange
≤24hrs 10-12 (7-10) 20 (18)
25-48hrs 12-15 (10-12) 20-25 (20)
49-72hrs 15-18 (12-15) 25-30 (>20)
>72hrs 18-20 (12-15) 25-30 (>20)
Bilirubin levels expressed in mg/dl
In brackets are Bili levels for infants with risk factors
*PEDIATRICS, 1994; 94:558-565 (modified)