JAUNDICE IN THE NEWBORN

FAFUNSO A.
RAJI A. S.
ONAGA A.I.

The authors are 3rd year Clinical Students of the College of Medicine, University of Ibadan.

NEONATAL JAUNDICE

This is the yellowish discolouration of the skin and mucous membranes and sclera in a neonate. It is the commonest symptom in the newborn period and is a manifestation of hyperbilirubinaemia. It becomes apparent when serum bilirubin is 5-7mg/dl.

Incidence

It is a common paediatric problem worldwide. It is the commonest clinical sign in the neonatal period and the commonest cause of neonatal admission in Nigeria. It accounts for 57% and 60% of neonatal admissions in UCH and LUTH respectively while the figures are 16.3% of neonatal and 16.8% of paediatric admission in ABUTH and UNTH respectively.

At least 25% of term neonates develop clinical jaundice while the figure can be up to 80% in preterm babies.

Bilirubin Metabolism

In the normal newborn, bilirubin concentration in serum is dependent on three factors - bilirubin synthesis, bilirubin metabolism (transport, uptake, conjugation or excretion) and bilirubin enterohepatic circulation.

Synthesis

Bilirubim is derived from the breakdown of heme-containing proteins. 1g of haemoglobin yields 34mg of bilirubim[2,3] (fig 1).

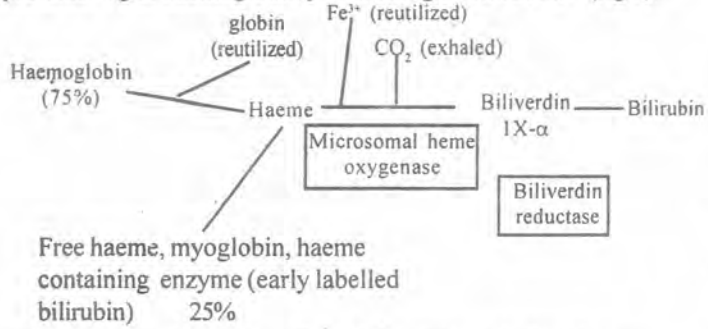

Figure 1 Bilirubin synthesis from Haemoglobin and other Haeme containing proteins

Transport, Uptake, Conjugation, Excretion

Figure 2 summarizes the 3 major processes involved in the transfer of bilirubin from blood to bile.

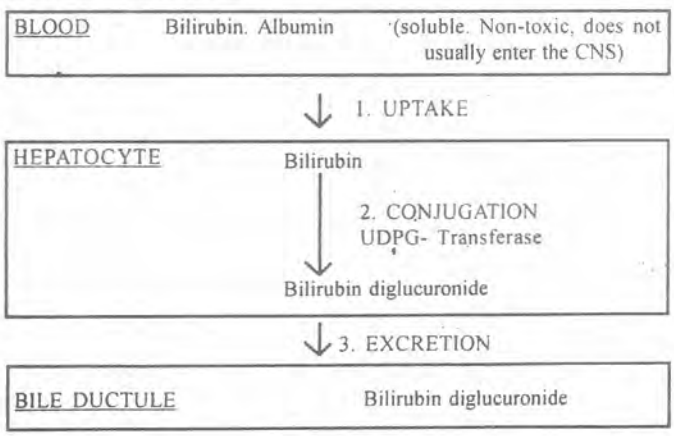

Figure 2 - Diagramatic representation of the 3 major processes (uptake, conjugation, and excretion) involved in the transfer of bilirubin from blood to bile. Certain intracellular proteins of hepatocytes, such as ligadin and Y protein are involved in the uptake of bilirubin by these cells.The conjugated bilirubin, bilirubin diglucoronide is water soluble and most of it makes its way through the biliary system into the gut at mid-duodenal level, and the pigment is subsequently reduced by fecal flora to urobilinogens, because the newborn gut is sterile. The reduction does not occur, and the newborn gut contains beta-glucuronidase, which hydrolizes bilirubin diglucoronide, producing unconjugated bilirubin that may be reabsorbed (Enterohepatic circulation). This partly explain the reason why newborn babies readily develop jaundice.[4,5,6].

Aetiology of Neonatal Jaundice[1,2,9]

A. Bilirubin Over Production

1. Intravascular Haemolysis (Unconjugated hyperbilirubinemia)

* Enzyme deficiencies (G-6-PD deficiency (commonest), Pyruvate kinase deficiency)
* Blood group Incompatibility e.g. ABO Rh.
* Abnormalities of red cells
- Hereditary Spherocytosis (elliptocytosis, Somatocytosis)
- Pyknocytosis
- Haemoglobinopathy (Alpha thalasemia, Delta-beta thalasemia, Barts)
- Polycythemia (large placenta transfusion, fetofetal transfusion, maternal-fetal transfusion)

2. **Extravascular hemolysis (concealed haemorrhage)** (Unconjugated hyper bilirubinemia)
- Haematoma e.g. cephalhaematoma, subgaleal, pulmonary or cerebral
- Ecchymosis
- Swallowed maternal blood

3. **Increased Enterohepatic circulation (Unconjugated hyperbilirubinemia)**

As it occurs in delayed passage of meconium from any course, such as:
- Pyloric Stenosis
- Hirschsprung's disease

B. Bilirubin undersecretion

1.Metabolic and endocrine conditions (mixed unconjugated and conjugated hyperbilirubinemia)
- Galactosemia
- Familial non-haemolytic jaundice type 1 and 2 (Crigler- Najjar syndrome)
- Gilbert's disease
- Hypothyroidism
- Tyrosinosis

- Hypermethionemia
- Drug and hormones (e.g. novobiocin, pregnanediol, Lucey-Driscoll) Syndrome
- Infants of Diabetic mothers
- Prematurity
- Hypopituitarism and Anencephaly

2. Obstructive Disorders (Conjugated hyperbilirubinemia)

- Biliary atresis
- Choledochal Cyst
- Cystic fibrosis (inspissated bile)
- Tumor or blood (extrinsic obstruction)

3. Alpha -1- antitrypsim deficiency
Parenternal Nutrition

C. Mixed Course
- Sepsis
- Introuterine infections - TORCHES, Hepatitis, Coxsaekie
- Respiratory distress syndrome
- Asphyxia
- Infant of diabetic mother

Jaundice may not be seen in the Neonatal period.

Physiologic Jaundice

Serum Unconjugated bilirubin in most well full-term neonates rises above 2mg/dl shortly after birth to peak at 6 to 8mg/dl between the fourth and fifth day of life and then drops rapidly in the next 2 days, thereafter slowly over the next few days till about 2 weeks of age when adult level of < 2mg/dl is reached. A rise to 12.5mg/dl is accepted as being in the physiologic range though it has been reported that up to 6% of well term neonates have values above 12.5mg/dl and another 3% of neonates have values above 15mg%.

In premature infants, the peak may be 10 to 12mg/dl on the 5th day of life, possibly rising over 15mg/dl without any specific abnormality of bilirubin metabolsim. Level under 2mg/dl may not be seen until one month of age in both full-term and premature infants. This normal jaunduce is called PHYSIOLOGIC JAUNDICE, and it often manifest from 48 hours of age and clears by 7 days of age.

Physiologic Jaundice is a diagnosis of exclusion which is made only after pathologic causes have been excluded. It is caused by:

a. An Increased bilirubin load presented to the liver cells due to:
   i. increased RBC volume per kg as compared adult.
   ii. decreased survival of fetal RBC: 90 day - Survival as compared with 120 days in adult.
   iii. increased early - labelled bilirubin.
   iv. increased enterohepatic circulation.

b. Liver cell immaturity and thus decreased ligandin and UDP-Glucoronyl transferase activity[2].

Breast Milk Associated Jaundice

There are two types of breast feeding problems that are related to neonatal hyperbilirubinemia.

1. Breat Milk Jaundice[1,2]

This is of late onset and occurs in about 1% of breast-fed infants. It is due to enhanced reabsorption of unconjugated bilirubin due to an unidentified factor which seems present in majority of human milk and bilirubin level may rise up to 20 to 30mg/dl in the if breast feeding is continued. If breast feeding is stopped, the bilirubin will fall rapidly in 48 hours.

Factors suggested as likely causes include the following:
a. hormone (3-alpha, 20-beta pregnanediol in some mother's breast milk, inhibiting bilirubin conjugation.
b. Higher lipoprotein lipase activity, releasing free fatty acids which interfere with hepatic uptake or bilirubin conjugation.
c. Increases resorption of bilirubin from the stool due to:
   (a) Increase B-glucuronidase activity in breast milk
   (b) Decrease passage of stool due to less stool volume.

2. Breast feeding Jaundice (of early onset)

This exaggeration in physiological jaundice is related to inadequate breast milk intake and faulty breast feeding techniques which accentuates enterohepatic recirculation of bilirubin. treatment consists of establishing proper feeding techniques, breast milk production, ensuring breast feeding frequencies are adequate (10-12 times per day) and avoiding water or glucose-water supplements.[1]

Pathologic Jaundice

This is jaundice due to an identifiable course may not be easy to distinguish from physiologic jaundice. The following may suggest non-physiologic jaundice and require investigation.[5,7,8]

1. Jaundice in any sick neonate
2. Clinical jaundice prior to 36 hours of age
3. Serum bilirubin concentrations increasing by more than 5mg/dl per day (or >0.5mg/dl/hour)
4. Total Serum bilirubin level greater than 17mg/dl in a breast fed or 15mg/dl in a formula-fed term infant
5. Clinical jaundice persisting after 7 days in a term infant or after 14 days in a premature infant.
6. Conjugated Serum bilirubin >1.5mg/dl.

Management

Regardless of aetiology, the goal of therapy is to prevent the concentration of indirect reacting bilirubin in the blood from reaching levels at which neurotoxicity may occur.

Modalities of treatment include:
* Phototherpy
* Exchange transfusion

They are the 2 main modalities of treatment that are widely employed to keep the maximum total serum bilirubin level indicated in table 1:-

Table 1: Suggested maximum indirect Serum bilirubin Concentrations (mg/dl in Infants)

Birthweight(g)	Uncomplicated	Complicated
<1000	12-13	10-12
1000-1250	12-14	10-12
1251-1499	14-16	12-14
1500-1999	16-20	15-17
2000-2500 and above	20-22	18-20

Phototherapy is usually started at 50-70% of maximum indirect serum bilirubin levels as shown above.

Exchange transfusion in these patients is indicated if:-

(a) Values of serum bilirubin greatly exceed the above listed values.
(b) phototherapy is unsuccessful in reducing the maximum bilirubin level.
(c) There are signs of kernicterus

Complications in the table refers to those patients with any of the following : Perinatal asphyxia, acidosis, hypoxia, hypothermia, hypoalbuminemia, meningitis, intraventricular haemorrhage, haemolysis and hypoglycaemia.

In developed countries due to availability of facilities for regular monitoring of babies with neonatal jaundice, phototheraphy and Exchange blood transfusion are deffered till higher valuesof serum bilirubin than shown in table 1 above, for babies without ongoing haemolysis

Phototheraphy.

Clinical jaundice and indirect hyperbilirubinemia reduced on exposure to a high intensity of light in the visible spectrum.

Phototheraphy is most effective when white light in the broad-spectrum range is placed at an optimal distance of 45cm from the patient. Phototherapy acts by:-

(a) photoisomerizing bilirubin in the skin into an isomer which in non-toxic and excreted in the bile
(b) photoreduction of bilirubin to lumirubin which is also non-toxic and excreted by the kidney in the unconjugated state.

Conventional phototherapy is applied continuously and the infants is turned frequently for maximal exposure. The infants eyes should be closed and adequately covered to prevent exposure to light. The gonads should be covered as well and body temperature should be monitored. The advent of fiberoptic phototherapy units which also provide continuous photheraphy have made it possible to manage a baby on an outpatient basis.

Exchange Blood Transfusion

This widely accepted treatment should be repeated as frequently as necessary to keep indirect serum bilirubin levels below those noted in Table 1.

Exchange blood transfusion involves exchanging twice the blood volume of the body, with fresh whole blood. Double volume Exchange blood transfusion will reduce circulating serum bilirubin by about 80%.

However, it is important to emphasize that it is important to determine aand treat concomitantly the basic cause(s) of the jaundice.

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