International Journal of Pharmacology and Clinical Research (IJPCR)

IJPCR |Volume 2 | Issue 1 | Jan – Jun- 2018
www.ijpcr.net

Review article *Clinical research*

ISSN: 2521-2206

Neonatal jaundice- a review article

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ABSTRACT

Neonatal jaundice is the condition often seen in infants around the second day after birth. It is mainly caused by increased levels of bilirubin (physiological jaundice and prolonged jaundice and other non organic causes) and the symptoms like yellow colour of the skin, dark urine, pale stools. It was assessed by colour of the skin and severity of jaundice (krammers staging score).Treated by phototherapy, exchange transfusion, pharmacological agents and natural and home remedies. By this article we concludes that parents should be educated about the consequences of severe hyperbilirubinemia and simple means to prevent it.

Keywords: Hyperbiliruinemia, Jaundice, Phototherapy, Natural remedies.

INTRODUCTION

Jaundice is the condition which is characterised by yellowish or greenish pigmentation of the skin and whites of the eyes due to high bilirubin levels. It is commonly associated with itchiness. The term “Jaundice” comes from the French language and means “yellow”. The most common alternative name for jaundice is Icterus. Other terms include Yellow Skin and Yellow Eyes. This condition is most commonly found in new-born and infants, however, it affects adults as well. The faeces may be pale in colour and the urine becomes dark. Jaundice is caused due to the accumulation of bilirubin (a yellow pigment) in the skin. When blood cells complete their life cycle, they are broken down in the body. Bilirubin from these cells is released, which further gets filtered in the liver and then excreted. Since the liver of the baby is not fully developed, it cannot filter the entire bilirubin formed, which thus accumulates in the skin, resulting in neonatal jaundice [1]. If bilirubin levels in babies are very high for too long, a type of brain damage known as kernicterus may occur [2]. In neonates, the evaluation of sclera is difficult due to the presence of physiological photophobia [3].

TYPES OF JAUNDICE

There are three types of jaundice

1. Haemolytic jaundice –It is caused by destruction of red blood cells. This causes increased bilirubin formation and anaemia
2. Obstructive jaundice –It is caused by a blockage in the pathway where bilirubin is made in the

liver cells and where bile goes into the duodenum

3. Hepatocellular jaundice –It is caused by damage to liver cells. The damage could be from a viral infection or toxic drugs.

Yellow discoloration of the skin and the whites of the eyes happens in all types of jaundice [4].

NORMAL VALUE OF BILIRUBIN

BILIRUBIN	NORMAL VALUE
New Born	0.8 to 12.0 mg/dl
Abnormal Value New-born	>15mg/dl
FecalUrobilinogen	40 to 280 mg/day
Urine	0.0 to 0.02mg/dl

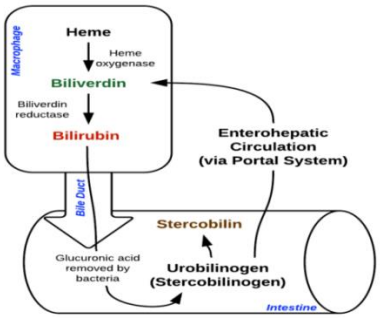
NEONATAL JAUNDICE

Neonatal jaundice (or) neonatal hyperbilirubinemia, (or) neonatal icterus this condition is often seen in infants around the second day after birth, lasting until day 8 in normal births, or to around day 14 in premature births [3]. In neonates, the yellow discoloration of the skin is first noted in the face and as the bilirubin level rises proceeds caudal to the trunk and then to the extremities. Icteric, is a yellowing of the skin and other tissues of a newborn infant. A bilirubin level of more than 85 μmol/l (5 mg/dL) leads to a jaundiced appearance in neonates. This condition is common in newborns affecting over half (50–60%) of all babies in the first week of life. Neonatal jaundice can make the newborn sleepy and interfere with feeding. Extreme jaundice can cause permanent brain damage from kernicterus [5].

Physiology of bilirubin

Bilirubin (formerly referred to as haematoidin and discovered by Rudolf Virchow in 1847) is a yellow compound that occurs in the normal catabolicpathway involving breakdown of heme in vertebrates. This catabolism is a necessary process in the body's clearance of waste products that arise from the destruction of aged red blood cells. First, the hemoglobin gets stripped of the heme molecule which thereafter passes through various processes ofporphyrin catabolism, depending on the part of the body in which the breakdown occurs. The production of biliverdin from heme is the first major step in the catabolic pathway, after which the enzyme biliverdinreductase performs the second step, producing bilirubin from biliverdin [5].

1gm of Haemoglobin results in the production of 34mg bilirubin.
A normal new born produces 6 to 10mg/kg/day of bilirubin.



Bilirubin is excreted in bile and urine, and elevated levels may indicate certain diseases. It is responsible for the yellow color of bruises and the yellow discoloration in jaundice. Its subsequent breakdown products, such as stercobilin, cause the brown color of faeces. A different breakdown product, urobilin, is the main component of the straw-yellow color in urine. There is unconjugated bilirubin and conjugated bilirubin. In the liver, bilirubin is conjugated with glucuronic acid by the enzyme glucuronyl transferase, makingit soluble in water: the conjugated version is the main form of bilirubin present in the "direct" bilirubin fraction. The measurement of unconjugated bilirubin depends on its reaction with diazosulfanilic acid to create azobilirubin. [5]

What happens when new born has jaundice

Red blood cells die off in large numbers after death

⬇

A lot of bilirubin is produced

⬇

Because the liver is not yet mature, it processes bilirubin

⬇

Very little bilirubin leaves the body

⬇

The excess, unprocessed bilirubin builds up everywhere in the body it colours the skin and eyes become yellow.

SIGNS AND SYMPTOMS

- Drowsiness
- Pale stools - breast-fed babies should have greenish-yellow stools, while those of bottle fed babies should be a greenish-mustard color
- Poor sucking or feeding
- Dark urine - a new born's urine should be colourless(Brown urine)
- Yellow colour of the skin
- High pitch cry
- Vomiting [6].

CAUSES OF NEONATAL JAUNDICE

Physiological jaundice

It is attributable to physiological immaturity usually appears between 24 to 74 hours of age and peaks by 4 to 5 days in term of 7th day in preterm neonates and disappears in 10 to 24 days of life. This is predominately unconjugated bilirubin levels, usually, does not exceed 15mg/dl[4]. Most infants develop visible jaundice due to elevation of unconjugated bilirubin concentration during their first week. This pattern of hyperbilirubinemia has been classified into two functionally distinct periods [6].

Phase one

1. Term infants - jaundice lasts for about 10 days with a rapid rise of serum bilirubin up to 204 µmol/l (12 mg/dL).
2. Preterm infants - jaundice lasts for about two weeks, with a rapid rise of serum bilirubin up to 255 µmol/l (15 mg/dL).

Phase two

Bilirubin levels decline to about 34 µmol/l (2 mg/dL) for two weeks

1. Preterm infants - phase two can last more than one month.
2. Exclusively breastfed infants - phase two can last more than one month

Prolonged jaundice

Jaundice that lasts until and after 14 days after birth (or 21 days for premature babies) is called prolonged jaundice. It may indicate a serious problem but is most often caused by breast-feeding [6].

Non organic causes

Breast feeding jaundice

"Breastfeeding jaundice" or "lack of breastfeeding jaundice," is caused by insufficient breast milk intake, resulting in inadequate quantities of bowel movements to remove bilirubin from the body. This leads to increased enterohepatic circulation, resulting in increased reabsorption of bilirubin from the intestines. Usually it occurs in the first week of life. Most of the cases can be ameliorated by frequent breastfeeding sessions of sufficient duration to stimulate adequate milk production.

Breast milk jaundice:

Breastfeeding jaundice is a mechanical problem; breast milk jaundice is a biochemical occurrence and the higher bilirubin possiblyacts as an antioxidant. Breast milk jaundice occurs later in the newborn period, with the bilirubin level usually peaking in the sixth to 14thday of life. This late-onset jaundice may develop in up to one third of healthy breastfed infant [5].

Hemolytic jaundice

The common cause of hemolytic jaundice include Rh haemolytic disease, ABO incompatability,G-6PD deficiency, and minor blood incompatibility.

CLINICAL ASSESSMENT OF JAUNDICE

- Colour of the skin (to be checked in naked baby, naturalligt, non-yellow background, minimum blanching over bony surfaces)
- Severity of jaundice (krammers staging of jaundice)
- Anemia, signs of dehydration.
- Hepatospleenomegaly
- Complete neurological examination to look for s/o of kernectirus.
- Special look for cephalohematoma, bruisings or bulging of AF.
- Abdominal mass of distension

Kramers staging score

Area of body	Serum bilirubin levels	Score
Face	4-6mg/dl	1
Chest ,upper abdomen	8-10mg/dl	2
Lower abdomen,thighs	12-14mg/dl	3
Arms,lower legs	15-18mg/dl	4
Palms,soles	15-20mg/dl	5

TREATMENT

Hyperbilirubinaemia can be treated with:

- Phototherapy
- Exchange transfusion
- Pharmacological agents

PHOTOTHERAPY

The phototherapy was first discovered, accidentally, at Rochford Hospital in Essex, England. Infants with neonatal jaundice are treated with colored light called phototherapy, which works by changing trans-bilirubin into the water solublecis-bilirubin isomer [5].

There are two types of phototherapy

- Conventional phototherapy: In non-haemolytic jaundice conventional phototherapy used.
- Intensive phototherapy: Intensive phototherapy is preferred when there is rapidly raised bilirubin levels and in haemolytic jaundice cases and ineffective of conventional phototherapy [3].

The main goal of therapy is to lower the concentration of circulating bilirubin or keep it from increasing. Phototherapy achieves this by using light energy to change the shape and structure

of bilirubin converting it to molecules that can be excreted even when normal conjugation is deficient. Absorption of light by dermal and subcutaneous bilirubin induces a fraction of the pigment to undergo several photochemical reactions that occur at very different rates. These reactions generate yellow stereoisomers of bilirubin and colourless derivatives of lower molecular weight. The products are less lipophilic than bilirubin, and unlike bilirubin, they can be excreted in bile or urine without the need for conjugation [6].

Phototherapy is carried out in different methods

	Light bank	Bilibed	Biliblanket
Equipment	Isolette/open cot according to unit policy. May be used in conjunction with a biliblanket.	Open cot or as per manufacturer's recommendation. Consider adding/changing to bank of lights if total serum bilirubin level continues to rise.	Open cot or in conjunction with light bank in isolette. May be used in conjunction with a bank of lights.
Clothing	Remove all clothing except disposable nappy. No lotions/lubricants on skin.	Remove all clothing except disposable nappy. Dress only in manufacturer's jumpsuit to maximise exposure to light. No lotions/lubricants on skin.	Remove all clothing except disposable nappy. Place fiberoptic pad between skin and singlet. No lotions/lubricants on skin.
Temperature	Hourly for first 4 hours then 3 – 4 hourly.10 Phototherapy may lead to an elevated isolette temperature. Do not turn the isoletteoff, it is not safe to nurse a baby in an isolette that has been turned off as air no longer circulates. Cover temperature probe with reflective disc if servo control method is used to monitor temperature.	Hourly for first 4 hours then 3 – 4 hourly.10	Hourly for first 4 hours then 3 – 4 hourly.10
Other observations	As per clinical condition and/or maturity. Check for skin rashes. Report dark urine and/or light (pale) stools.		
Eye patches	Required to protect immature retina.1,9 Monitor hourly to check for eye discharge. Remove with feeds/cares.10 Replace after feeds/cares before commencing phototherapy.	Not required.	

Feeds	Demand feeds if breastfeeding or at least 3 - 4 hourly or as age appropriate. Observe breastfeeding. Document input output. Weigh daily. May need to increase daily fluid volume intake.	Demand feeds if breastfeeding or at least 3 - 4 hourly. Observe breastfeeding. Document input output. Weigh daily.	Demand feeds if breastfeeding or at least 3 - 4 hourly. Observe breastfeeding. Document input output. Weigh daily.
Position	Position babies under phototherapy supine at all times in accordance with safe Infant sleeping guidelines.11 All babies nursed in neonatal units should only be placed in the prone position if continuous cardiorespiratory monitoring is used.11		
Bilirubin measurements	Switch off light during blood collection.		

Complications of phototherapy

- ✓ Babies with congenital erythropoietic porphyria can develop severe blistering and photosensitivity during phototherapy. Congenital porphyria or a family history of porphyria is a contraindication to the use of phototherapy.
- ✓ Intestinal hypermotility, diarrhoea.
- ✓ Separation of mother and baby causing interference of mother baby interaction (if facility is unable to keep mother and baby together while baby receives phototherapy).
- ✓ Parents find eye patching disturbing.
- ✓ Changes in the baby's thermal environment lead to increased peripheral blood flow and insensible water loss.
- ✓ Babies with cholestatic jaundice may development 'bronze baby syndrome' and rarely purpura and bullous eruption.
- ✓ Concomitant use of certain drugs or agents may cause photosensitivity [7].

EXCHANGE TRANSFUSION

This treatment is used when bilirubin levels are extremely high or are increasing too quickly to be treated by phototherapy **.**It is removing the infant's blood and replacing it with blood matched for blood group that is free of bilirubin. Extremely high levels of bilirubin can injure the brain (kernicterus) and lead to severe neurological impairment [8]. Immediate exchange transfusion is recommended even if the total serum bilirubin level is falling if a baby is jaundiced and displays signs of intermediate to advanced stages of acute bilirubin encephalopathy which include:

- Lethargy, hypotonia, poor feeding with high pitched cry
- Hyper alert or irritable
- Hypertonia, arching, retrocollis- opisthotonos
- Obtunded to comatose, apnoea, seizures

As blood collected after an exchange transfusion is of no value for investigating many of the rarer causes of severe hyperbilirubinemia, these investigations should be considered before performing exchange transfusion.

PHARMACOLOGICAL TREATMENT

Intravenous Immunoglobulin (IVIG)

IVIG reduces bilirubin concentrations in babies with rhesus haemolytic disease and other immune haemolytic jaundice. Babies with a positive DAT who have predicted severe disease based on antenatal investigation or have an elevated risk of progressing to exchange transfusion based on the postnatal progression of total serum bilirubin levels, should receive IVIG.1 The dose required is 1 g/kg1 given intravenously over 2 hours.

The use of IVIG may be recommended in special circumstances such as:

- Parental refusal for exchange transfusion
- Where appropriate blood components for exchange transfusion are unavailable

Phenobarbitone

May improve bile flow but is not recommended for treatment of hyperbilirubinaemia. It improves

hepatic uptake conjugation and excretion of bile flow and reduces bilirubin level. When used prophylactically in a dose of 5mg/kg for 3 to 5 days after birth it was shown to be effective in babies with hemolytic disease , extravascular blood and in preterms without any significant side effects. [3]

Ursodeoxycholic acid

May improve bile flow and lower bilirubin concentrations. Use only after discussion with a Neonatologist and/or gastroenterologist [7].

Hemeoxygenase inhibitors

The rate-limiting step in bilirubin production is the conversion of heme to biliverdin by hemeoxygenase. Certain synthetic metalloporphyrins are powerful competitive inhibitors of hemeoxygenase and suppress the formation of bilirubin. One such compound that has been studied extensively is tin mesoporphyrin (SnMP). A series of controlled clinical trials have demonstrated that SnMP is a potent inhibitor of hemeoxygenase and is highly effective in reducing TSB levels and the requirements for phototherapy in term and preterm neonates. The only reported adverse effect has been a transient erythema that disappeared without sequelae in infants who received white light phototherapy after SnMP administration. This drug isstill awaiting approval by the US Food and Drug Administration, although it can be obtained for compassionate use (InfaCare Pharmaceutical Corp, Trevose, PA, USA). If approved, SnMP could find immediate application in preventing the need for exchange transfusion in infants who are not responding [7].

NATURAL REMEDIES COMMONLY USED TO TREAT JAUNDICE

Herbal Remedies

Several herbs have been used for hundreds of years to help buildup a strong liver. These herbs can also help fight against jaundice. Some commonly used herbs include:

1. Bitter Luffa
2. Radish Leaves
3. Tomatoes
4. Snake Gourd Leaves
5. Pigeon Pea Leaves
6. Sugarcane Juice
7. Lemon Juice
8. Barley Water
9. Jaundice Berry (also known as Berberisvultaris)

Most of these herbs can be found at a local Herbologist's or Naturalist's office, and some can be found at general nutrition centers and department stores. Proper home care of jaundice is best provided by receiving adequate physical rest. Recovery is dependent upon the liver being able to handle the amount of bilirubin from destroyed blood cells. Blood cells are destroyed less when a person is sleeping or resting than when they are physically active. Patients should drink plenty of juice of all kinds throughout the day and be on a light carbohydrate diet [39].

Home Remedies

Expose to Sunlight

In case of slight jaundice, treatment may not be required. However, the following step after consulting your doctor can be tried out. You should place your baby in sunlight for around fifteen minutes every day, at least 4 times a day. The baby's skin should be exposed and the glass window should be closed to filter sunlight. The bilirubin in the skin gets dissolved due to the sunlight and gets excreted through urine.

Home-Lamp Therapy

This therapy can be tried when the bilirubin level is increasing instead of reducing and it is an alternative treatment to keeping the baby in the hospital. If the bilirubin levels are unusually high, keep the baby under special sun lamp. A new type of treatment is to wrap the baby in a bili-blanket which reduces the bilirubin. This is a very easy way of home treatment for mild case of jaundice.

Frequent Feeding

Hydration is essential for flushing out excess bilirubin from the body. For this reason, frequent breast-feeding is very essential. Initially less milk is produced and breast-feeding frequency is also less which can be a contributing factor for early jaundice. If the frequency is increased, milk production also increases. Baby should be fed every 2 -3 hours and when he wakes up at night. In case the breast milk is inadequate, formula

supplements might be required to increase hydration and help in the excretion of bilirubin.

Feeding of Wheat Grass Juice

Wheat grass juice increases the enzymatic action in the liver and improves the ability of the liver to remove excess bilirubin from the body. Wheat grass juice can be added to the formula given to the baby. Around 20 drops per day of juice added to the formula work swell. Alternatively, the mother can drink 2 ounces of juice every day which will pass on to the baby through breast milk. This can be continued till jaundice fades and also helps prevent jaundice.

Providing Herbal Supplements to the Mother

Supplements like Dandelion tea, catnip, comfrey leaf and agrimony contain certain substances which help in detoxifying. The mother can take these supplements so that it can pass on to the baby through the breast milk. These natural detoxifiers help in flushing out the excess bilirubin from the baby's body. Mother should continue breast-feeding so that this mild treatment continues to work and help in getting rid of jaundice.

Temporary Stoppage of Breast Feeding

If the doctor informs you that the jaundice has occurred due to breast milk, you might have to temporarily discontinue feeding your baby. To ensure that you continue to produce breast milk, you can pump your breast every day and start breast feeding once the doctor gives you permission to. [7]

Surgical Treatments For Jaundice

Gall stones can often be the cause of jaundice in adults. In this case, a surgeon may opt to remove the gallstone and remove any excess bile from the patient. Blood transfusions can be performed on infants and adults who experience sever jaundice. Aside from these cases, surgery is not necessary in the treatment of jaundice. In the case of a severe liver problem that is also accompanied by jaundice, the patient may be required to have a liver transplant. [1]

REVIEW LITERATURE

Bolajoko O. Olusanya et al Maternal detection of neonatal jaundice during birth hospitalization using a novel two-colouricterometer. Some 2492 mother-infant pairs were enrolled over 15 months, of which 347 (13.9%) chose Dark Yellow. The mean TcB for Dark Yellow (10mg/dL) was significantly higher ($p<0.001$) than for Light Yellow (6.1mg/dL). Bilistrip™ showed increasing sensitivity (47.0% - 92.6%) and negative predictive value (NPV) (91.4% - 99.9%) for selected TcB thresholds (≥10mg/dL, ≥12mg/dL, ≥15mg/dL, and ≥17mg/dL). Among neonates with TSB measurements (n = 124), Bilistrip™ was associated also with increasing sensitivity (86.8% - 100%) and NPV (62.5% - 100%). The sensitivity and NPV for detecting neonates requiring phototherapy were 95.8% respectively. Only one of the 24 neonates who required phototherapy was missed by the Bilistrip™.They concluded that Bilistrip™ is a potential decision-making tool for empowering mothers to detect neonates with clinically significant jaundice that may require close monitoring or treatment, and neonates not requiring treatment for jaundice in the first week of life[10].

Vinod K. Bhutani et al studied Identification of neonatal haemolysis: an approach to pre discharge management of neonatal hyperbilirubinemia. Relative contributions of increased production [by end-tidal carbon monoxide concentrations (ETCOc)] and decrease elimination of bilirubin to pre discharge hour specific total bilirubin (TB) levels were assessed in healthy late-preterm and term new borns. Secondly, they report pre discharge ETCOc ranges to guide clinical management of hyperbilirubinemia. TB and ETCOc (≤3 time points) determinations of new borns aged between six hours and <6 days (n = 79) were stratified by postnatal age epochs. Hyperbilirubinemia risk was assessed by plotting TB values as a function of ETCOc. Stratifications of ETCOc (in ppm, mean, median and interquartile ranges) by postnatal age epochs (0–24, 24–48 and 48–72) were as follows: 2.0, 1.9, 1.8–2.2 (n = 11); 1.6, 1.5, 1.1–2.0 (n = 58); and 2.0, 1.8, 1.6–2.3 (n = 9), respectively. Infants with ETCOc≥ 2.5 were at high risk, between 1.5 and 2.5 at moderate risk and ≤1.5 were at low risk. Risk due to haemolysis alone was not independent ($p < 0.01$). For infants with TB >75th percentile (n = 31), 23% had ETCO ≤1.5, and 77% had ETCOc> 1.5 ($p < 0.00003$). Finally they concluded that Near-simultaneous ETCOc and TB measurements in infants with TB >75th

percentile accurately identify haemolytic hyperbilirubinemia [11].

***Sanjiv B Amin* et al** studied auditory toxicity in late preterm and term neonates with severe jaundice. They compared TSB, bilirubin: albumin molar ratio (BAMR), and unbound bilirubin for their association with auditory toxicity in neonates with severe jaundice (TSB ≥342lmol/L, or that met exchange transfusion). Twenty-eight out of 100 neonates (mean gestational age 37.4wks; 59 males, 41 females) had auditory toxicity. Peak unbound bilirubin, but not peak TSB and BAMR, was associated with auditory toxicity ($p<0.05$) in neonates with severe (TSB <427.5lmol/L) and extreme hyperbilirubinemia (TSB ≥427.5lmol/L). Area under the receiver operating characteristic curve for unbound bilirubin (0.78) was significantly greater ($p=0.03$) than TSB (0.54) among neonates with severe but not extreme hyperbilirubinemia. The mean peak TSB and unbound bilirubin for neonates were 24.2mg/dL (SD 4.9) and 1.84lg/dL (SD 1.91) respectively. Finally they concluded that Unbound bilirubin is more strongly associated with auditory toxicity than TSB and/or BAMR in greater or equal to 34 weeks gestational age neonates with severe jaundice. Unbound bilirubin is a better predictor than TSB in neonates with severe hyperbilirubinemia [12].

Shweta Singh et alA Study on Identification of Newborn at Risk of Hyperbilirubinemia in NCR, Delhi. Out of 205 neonates 51 developed peak serum bilirubin level more than or equal to 13 mg/dl while 154 neonates had serum bilirubin level below 13mg/dl. Thus, the incidence of hyperbilirubinemia was 24.8%. Neonatal factors like low gestational age, low birth weight, lower apgar score, history of jaundice in sibling and maternal factors like mothers' blood group, use of oxytocin and PROM are significantly associated with neonatal hyperbilirubinemia. In our study PROM >18 hours was associated with neonatal hyperbilirubinemia (p value of TSB levels = 0.013) which could be explained by increased risk of infection in a case of PROM , Use of oxytocin during labor irrespective of its dose and duration of use was related with hyperbilirubinemia they concluded that In resource limited healthcare settings, the cord-blood and clinical screening of the neonates with risk factors would prevent prolonged hospitalization and cost as well as readmission because of neonatal jaundice [13].

Sahoo et al studied the neonatal jaundice in a tertiary care centre of South India and they observed that Out of 560 new borns, 273 (48.8%) new borns developed clinical jaundice, 166 (61%) new borns developed physiological jaundice and 107 (39%) new borns developed non physiological jaundice they concluded that Breastfeeding jaundice tops the list in non physiological jaundice. it was stated that decreased volume and decreased frequency of feedings may result in mild dehydration and the delayed passage of meconium. (total serum bilirubin level above 12 mg per dL). ABO incompatibility has become the second most common cause of non physiological jaundice. Prematurity was third most common cause in our study. Preterm new borns are prone to developing jaundice due to immaturity of bilirubin conjugating system, higher rate of hemolysis, increased enter ohepatic circulation, decreased caloric intake [14].

Manjubala dash et al studied to assess the knowledge and attitude on neonatal jaundice among the mothers in a selected village of puducherry among the 50 mothers only one (2%) mother had adequate knowledge based on describes that 45(90%) of the mothers were able to identify the areas were yellowish discoloration occurs, 43(86%) were able to identify danger signs. In relation to their attitude it showed that 15(30%) mothers had positive attitude towards the management pattern of the baby on jaundice– that is taking the baby to hospital for treatment, continuing breast feeding etc. [15].

Girish N et al Evolving Trends: Hyperbilirubinemia among New borns Delivered to Rh Negative Mothers in Southern India. Anti-D prophylaxis and advances in neonatal care have reduced the frequency of HDN by almost a factor of 10 to 1 in 21,000 births. Out of 100 babies enrolled, 57 babies developed jaundice. Jaundice is 2.7 times more likely associated with babies born to multiparous Rh-ve mothers with $p=0.017$*. Jaundice is 3 times more likely associated with Rh+Ve babies born to multiparous mothers with $p=0.020$*. Jaundice is 3.97 times more likely associated with Rh+Ve babies born to multiparous mothers who have not received Anti-D with $p=0.154$. Treatment of jaundice is 2.75 times more

likely in Rh+ve babies born to multiparous mothers who have not received Anti-D with p=0.162. Duration of phototherapy is significantly more in Rh+ve babies born to multiparous mothers who had not received Anti-D with p=0.0097*.Exchange transfusion was required in two babies. In the present study, out of the 3 babies born to multiparous mothers in whom direct coombs test was positive, 2 babies had cord blood hemoglobin level of <11gm% with cord blood bilirubin level of >4.5mg%. Exchange transfusion was done in these 2 babies with subsequent phototherapy. One more baby had cord blood bilirubin level of >4.5mg% with cord blood hemoglobin level >11gm%. In this case, the mother's blood group was O-ve and the baby was B+ve. This baby was treated with double surface phototherapy only.They concludes that Although the incidence of Rh isoimmunization has declined dramatically over the years, it is still an important cause of neonatal morbidity and mortality emphasizing the need for more vigorous preventive efforts and up-to-date management skills [16].

Shaheena Kamal et al studied the Breast Non Feeding: Main Cause of Neonatal Hyperbilirubinemia in Areas Adjoining Shri Ram MurtiSmarak Institute of Medical Sciences, A Tertiary Care Teaching Hospital, Bareilly. 124 newborns with jaundice were enrolled in the study. Out of 124 cases of neonatal hyperbilirubinemia, 24 cases were of physiological jaundice,84- breast non feeding jaundice,5- breast milk jaundice, jaundice due to prematurity-5 and6- pathological jaundice. Insufficient caloric intake resulted from maternal and/or infant breast feeding difficulties may also increase unconjugated serum bilirubin concentration. There is history of hyperbilirubinemia in siblings of 30% of cases. Klebsiella & pseudomonas was detected in blood culture of two cases conferring the diagnosis of neonatal sepsis. TSH & T4 levels in neonatal hypothyroidism were highly abnormal. Reticulocyte count is highest in ABO incompatibility cases as hemolysis is maximum in these newborns. Conjugated bilirubin level & liver function tests were highly abnormal in case of congenital biliary atresia and finally they concluded that breast feeding/non feeding is the most common cause ofneonatal hyperbilirubinemia [17].

Shiyam Sundar Tikmani et al Incidence of neonatal hyperbilirubinemia: a population-based prospective study in Pakistan. Clinical assessments of jaundice were assigned by a physician and recorded using an adapted Kramer scale. Blood for plasma bilirubin was obtained if parents consented. Of a birth cohort of 1690 young infants during the study period, 466 infants (27.6%) were referred to our centre with jaundice. Of these, 64% were 0-6 days old. Bilirubin was measured in 125 of 466 (27%) jaundiced newborns. Overall detected rate of hyperbilirubinemia (bilirubin >5 mg/dl) among 1690 newborns was 39.7/1000 live births (95% CI 29.3–47.6). Rate of plasma bilirubin levels in the range of 15–20 mg/dl was 13/1000 live births (95% CI 7.6–18.4); levels >20 mg/dl were observed in 3.5/1000 live births (95% CI 0.4–5.5). The proportion of newborns with bilirubin ≥15 mg/dl was significantly higher among those assigned a Kramer score of 4–5 compared to those receiving a score of 1–3 (P value 0.00004).they concluded that A significant burden of untreated severe neonatal jaundice, causing potential neurological sequelae, exists in developing countries such as Pakistan. WHO guidelines are needed for screening and appropriate management of neonatal jaundice in developing countries [18].

KhalafMreihil et alstudied Early Isomerization of Bilirubin in Phototherapy of Neonatal Jaundice. Twenty jaundiced neonates were treated with phototherapy, and blood samples were drawn before and at ~15, 30, 60, and 120 min (10 infants) or at ≈15, 60, 120, and 240 min (10 infants) after beginning phototherapy for determination of TSB and 4*Z*, 15*E* photoisomers of bilirubin. Significant ($p < 0.0001$) formation of the 4*Z*, 15*E*photoisomer was detectable within 15 min. The change in TSB from time 0 was insignificant at 120 min but reached significance at 240 min ($p < 0.001$). The 4*Z*, 15 *E* bilirubin constituted up to 20–25% of TSB at 2 h and may not have peaked by 4 h.Further studies are needed to determine whether this early shift in balance between bilirubin isomers with different polarities may impact the risk of bilirubin encephalopathy even before TSB starts to fall [19].

PREVENTION

The best prevention of infant jaundice is adequate feeding. Breast-fed infants should have

eight to 12 feedings a day for the first several days of life. Formula-fed infants usually should have 1 to 2 ounces (about 30 to 60 milliliters) of formula every two to three hours for the first week.

CONCLUSION

Preterm newborns are prone to developing jaundice due to immaturity of bilirubin conjugating system, higher rate of hemolysis, increased enter hepatic circulation, decreased caloric intake. There are 30-40% of normal term newborns develop transient jaundice 3 to 5days after birth. The most common cause of occurring hyperbilirubinemia is inadequate breast feeding to the newborn. Parents should be educated about the consequences of severe hyperbilirubinemia and taught simple means to prevent it. Exclusive breast feeding without prolonged periods of fasting, and avoidance of supplementation with dextrose or water is some documented measures associated with lower serum bilirubin levels in newborns. Hence government and health service organisations should conduct workshops, seminars and lectures for mothers regarding neonatal jaundice.

ACKNOWLEDGEMENT

The authors are thankful for the management of Vishwabharathi College of Pharmaceutical Sciences, Perecherla, Guntur and A.P for providing facilities for carrying out this review article.

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