FACTORS AFFECTING BILIRUBIN LEVELS DURING FIRST 48 HOURS OF LIFE IN HEALTHY INFANTS

Harischandra Venkata Yanamandala[1], Seshagiri Koripadu[2]

[1]Associate Professor, Department of Paediatrics, Gitam Institute of Medical Sciences and Research, Rushikonda, Visakhapatnam.
[2]Assistant Professor, Department of Paediatrics, Gitam Institute of Medical Sciences and Research, Rushikonda, Visakhapatnam.

ABSTRACT

BACKGROUND

Neonatal jaundice or neonatal hyperbilirubinemia or neonatal icterus has originated from the Greek word ικτερος, icteric is 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, whereas in adults, a level of 34 µmol/L (2 mg/dL) is needed for this to occur. In newborns, jaundice is detected by blanching the skin with pressure applied by a finger, so that it reveals underlying skin and subcutaneous tissue. Jaundiced newborns have yellow discoloration of the white part of the eye and yellowing of the face extending down onto the chest.

The aim of the study is to evaluate the relation of various factors such as gestational age, type of delivery, feeding modalities, existence and type of maternal anaesthesia and first meconium passage time with early bilirubin levels during first 48 hours of healthy infants.

MATERIALS AND METHODS

This study was a prospective study, which was carried out in the Department of Paediatrics in Gitam Institute of Medical Sciences and Research, Rushikonda, Visakhapatnam, during the period of October 2015 to November 2016.

RESULTS

In the present study, 200 infants were involved. Foetal growth was small for gestational age in 8 infants (3%) appropriate for gestational age in 189 infants (95%) and large for gestational age in 3 infants (2%). Delivery mode was through vaginal mode in 82 infants (41%) and through caesarean section in 118 infants (59%). Anaesthesia type was general in 25 (12%), epidural anaesthesia in 19 (10%) and spinal anaesthesia in 156 (78%). Feeding type was breastfed in 162 (81%), mixed in 36 (18%) and formula in 2 (1%). Apgar score at 1 minute was 7 and at 5 minutes was 8. Gestational age was 36 weeks. Birth weight was 3125 grams, length was 52 cm and head circumference was 37 cm. The meconium passage time in vaginal delivery and caesarean delivery was 5 hours. Cord bilirubin was 1.5 mg/dL in both the delivery modes, 24 hrs. bilirubin levels were 4 g/dL in both the delivery modes and 48 hrs. bilirubin levels were 6.25 mg/dL in vaginal delivery and 6.3 mg/dL in caesarean delivery. The meconium passage time (11 hours) and cord bilirubin was highest (1.8 mg/dL) in general anaesthesia, 24 hrs. bilirubin was highest (4.4 mg/dL) in epidural anaesthesia and 48 hrs. bilirubin was highest (6.75 mg/dL) in spinal anaesthesia.

CONCLUSION

High cord bilirubin levels were associated to be in high-risk zone for later hyperbilirubinemia. Early bilirubin levels in healthy neonates were not associated to type of delivery or anaesthesia, late prematurity, feeding type and first meconium passage times.

KEYWORDS

Hyperbilirubinemia, Neonatal Jaundice, Alagille Syndrome.

HOW TO CITE THIS ARTICLE: Yanamandala HV, Koripadu S. Factors affecting bilirubin levels during first 48 hours of life in healthy infants. J. Evid. Based Med. Healthc. 2017; 4(91), 5435-5438. DOI: 10.18410/jebmh/2017/1087

BACKGROUND

Neonatal jaundice or neonatal hyperbilirubinemia or neonatal icterus has originated from the Greek word ικτερος, 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, whereas in adults, a level of 34 µmol/L (2 mg/dL) is needed for this to occur. In newborns, jaundice is detected by blanching the skin with pressure applied by a finger, so that it reveals underlying skin and subcutaneous tissue.[1] Jaundiced newborns have yellow discoloration of the white part of the eye and yellowing of the face extending down onto the chest. Neonatal jaundice can make the newborn sleepy and interfere with feeding. Extreme jaundice can cause permanent brain damage from kernicterus. In

Financial or Other, Competing Interest: None.
Submission 20-10-2017, Peer Review 29-10-2017,
Acceptance 12-11-2017, Published 21-11-2017.
Corresponding Author:
Dr. Seshagiri Koripadu,
No. 15-12-19/1, Flat No. 101, Padmalaya Apartments,
Krishna Nagar, Maharanipeta, Vishakhapatnam - 530002.
E-mail: seshagiri_neo@yahoo.co.in
DOI: 10.18410/jebmh/2017/1087

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.[2] This condition is common in newborns affecting over half (50-60%) of all babies in the first week of life.[3] Infants whose palms and soles are yellow have serum bilirubin level over 255 µmol/L (15 mg/dL) (more serious level). Studies have shown that trained examiners assessment of levels of jaundice show moderate agreement with icterometer bilirubin measurements. In infants, jaundice can be measured using invasive or non-invasive methods. In neonates, jaundice tends to develop because of two factors- the breakdown of foetal haemoglobin as it is replaced with adult haemoglobin and the relatively immature metabolic pathways of the liver, which are unable to conjugate and so excrete bilirubin as quickly as an adult. This causes an accumulation of bilirubin in the blood (hyperbilirubinemia) leading to the symptoms of jaundice. If the neonatal jaundice does not clear up with simple phototherapy, other causes such as biliary atresia, progressive familial intrahepatic cholestasis, bile duct paucity, Alagille syndrome, alpha-1 antitrypsin deficiency and other paediatric liver diseases should be considered. The evaluation for these will include blood work and a variety of diagnostic tests. Prolonged neonatal jaundice is serious and should be followed up promptly. In the first week of life of a neonate, neonatal jaundice is the most common cause of hospitalisation. Conjugation in the newborn liver, transport and developmental insufficiency of bilirubin uptake is the cause of physiological jaundice. The major contributing factors of hyperbilirubinemia is decreased, gut motility delayed passage of bilirubin rich meconium and absence of intestinal bacteria that deteriorates bilirubin to urobilinogen. The risk of hyperbilirubinemia is enhanced by delayed initiation of breastfeeding, technical problems in nursing may cause insufficiency of maternal milk. In most clinics, understanding the major contributing factors of early neonatal hyperbilirubinemia may be of help in identifying highest risk of hyperbilirubinemia. Hence, in this study, the relation of various factors such as gestational age, type of delivery, feeding modalities, existence and type of maternal anaesthesia and first meconium passage time with early bilirubin levels during first 48 hours of healthy infants.

MATERIALS AND METHODS

This study was a prospective study, which was carried out in the Department of Paediatrics in Gitam Institute of Medical Sciences and Research, Rushikonda, Visakhapatnam, during the period of October 2015 to November 2016. This study was conducted in infants born after 34 weeks of gestational age. Exclusion criteria was congenital anomaly, asphyxia, traumatic birth caused by extraction by vacuum, insufficiency in respiration, infection, haemolytic and metabolic diseases. Last menstrual period was used in determining the gestational ages. Total bilirubin levels, cord blood of all the infants involved in the study for 24 hours and 48 hours bilirubin levels were measured additionally. Total bilirubin levels were measured by using bilirubinometer with spectrophotometric method. Anaesthesia and delivery types, Apgar scores, birth weights, birth lengths and circumferences of head, gender, first feeding, first meconium passage times and mothers and child's blood groups were measured. Infants were classified into three groups as breastfed, formula-fed, mixed feeding (breastfed with formula support). A 12 mg 0.5% bupivacaine was used as routine anaesthesia for spinal anaesthesia, and for epidural anaesthesia, 0.5% levobupivacaine (18 mL) was used. Chi-square test was used for data analysis.

RESULTS

This study included 200 infants.

Variable		Number (%)
Gender	Females	85 (43%)
	Males	115 (57%)
Foetal growth	Small for gestational age	8 (3%)
	Appropriate for gestational age	189 (95%)
	Large for gestational age	3 (2%)
Delivery mode	Vaginal	82 (41%)
	Caesarean Section	118 (59%)

Table 1. Demographics in Infants

Table 1 shows that females were 85 (43%), males were 115 (57%). Foetal growth was small for gestational age in 8 infants (3%), appropriate for gestational age in 189 infants (95%) and large for gestational age in 3 infants (2%). Delivery mode was through vaginal mode in 82 infants (41%) and through caesarean section in 118 infants (59%).

Variable		Number (%)
Anaesthesia type	General	25 (12%)
	Epidural	19 (10%)
	Spinal	156 (78%)
Feeding type	Breastfed	162 (81%)
	Mixed	36 (18%)
	Formula	2 (1%)
Apgar score	At 1 minute	7
	At 5 minutes	8

Table 2. Demographics in Infants

Table 2 shows that anaesthesia type was general in 25 (12%), epidural anaesthesia in 19 (10%) and spinal anaesthesia in 156 (78%). Feeding type was breastfed in 162 (81%), mixed in 36 (18%) and formula in 2 (1%). Apgar score at 1 minute was 7 and at 5 minute was 8. Gestational age was 36 weeks. Birth weight was 3125 grams, length was 52 cm and head circumference was 37 cm.

Delivery Mode	Vaginal (n=82)	Caesarean Section (n=118)
Meconium passage (hrs.)	5	5
Cord bilirubin (mg/dL)	1.5	1.5
24 hrs. bilirubin (mg/dL)	4.0	4.0
48 hrs. bilirubin (mg/dL)	6.25	6.3

Table 3. Shows Relationship of Delivery Modes and Meconium Passage Times and Bilirubin Levels

Table 3 shows that meconium passage time in vaginal delivery and caesarean delivery was 5 hours. Cord bilirubin was 1.5 mg/dL in both the delivery modes, 24 hrs. bilirubin

levels were 4 g/dL in both the delivery modes and 48 hrs. bilirubin levels were 6.25 mg/dL in vaginal delivery and 6.3 mg/dL in caesarean delivery.

Delivery Mode	General Anaesthesia (n=25)	Epidural Levobupivacaine (n=19)	Spinal Bupivacaine (n=156)
Meconium passage (hrs.)	11	6	7
Cord bilirubin (mg/dL)	1.8	1.6	1.7
24 hrs. bilirubin (mg/dL)	3.9	4.4	4.1
48 hrs. bilirubin (mg/dL)	6.6	6.7	6.75

Table 4. Shows Relationship of Meconium Passage Time and Bilirubin Levels with Anaesthesia Type

Table 4 shows that the meconium passage time and cord bilirubin was highest in general anaesthesia; 24 hrs. bilirubin was highest in epidural anaesthesia; and 48 hrs. bilirubin was highest in spinal anaesthesia.

DISCUSSION

In the present study, 200 infants were involved. Females were 85 (43%) and males were 115 (57%). Foetal growth was small for gestational age in 8 infants (3%), appropriate for gestational age in 189 infants (95%) and large for gestational age in 3 infants (2%). Delivery mode was through vaginal mode in 82 infants (41%) and through caesarean section in 118 infants (59%). Anaesthesia type was general in 25 (12%), epidural anaesthesia in 19 (10%) and spinal anaesthesia in 156 (78%). Feeding type was breastfed in 162 (81%), mixed in 36 (18%) and formula in 2 (1%). Apgar score at 1 minute was 7 and at 5 minutes was 8. Gestational age was 36 weeks. Birth weight was 3125 grams, length was 52 cm and head circumference was 37 cm. The meconium passage time in vaginal delivery and caesarean delivery was 5 hours. Cord bilirubin was 1.5 mg/dL in both the delivery modes, 24 hrs. bilirubin levels were 4 g/dL in both the delivery modes and 48 hrs. bilirubin levels were 6.25 mg/dL in vaginal delivery and 6.3 mg/dL in caesarean delivery. The meconium passage time (11 hours) and cord bilirubin was highest (1.8 mg/dL) in general anaesthesia, 24 hrs. bilirubin was highest (4.4 mg/dL) in epidural anaesthesia and 48 hrs. bilirubin was highest (6.75 mg/dL) in spinal anaesthesia. Similar studies were conducted by Betul Siyah Bilgin et al[4] conducted a study in which infants born with caesarean section were fed later and more often had mixed feeding. First meconium passage was delayed with general anaesthesia. Cord, 24 and 48 hours' bilirubin levels were not correlated with first feeding time, meconium passage time, mode of delivery, existence and type of anaesthesia and feeding modalities. Being in high intermediate risk zone at 72 hours of Bhutani's nomogram was only related to first feeding time and high cord bilirubin level. Late preterm infants were more frequently born with caesarean section and offered supplementary formula. Therefore, first meconium passage times and bilirubin levels were similar in the late preterm and term infants. This study concluded that type of delivery or anaesthesia, late prematurity, feeding modalities and first meconium passage time were not related to early bilirubin levels in healthy neonates, but delayed first feeding and high cord bilirubin levels were related to be in higher risk zone for later hyperbilirubinemia. Ahmad Shah Farhat et al[5] conducted a prospective, cross-sectional study was conducted in 2012 in Emam Reza Hospital of Mashhad, Iran, 2012. In all term infants, who met the inclusion criteria, serum bilirubin level was measured by the bilitest device between the second and seventh days after birth. In cases with skin, bilirubin level >5 mg/dL, serum bilirubin was also checked. The collected data were analysed using SPSS, version 16. A total of 182 neonates were enrolled in the study, 56% of whom were male. The mean bilirubin levels in the NVD and CS groups were 9.4 ± 2.9 mg/dL and 9.8 ± 3.4 mg/dL, respectively (P=0.53). Additionally, comparison of the mean bilirubin levels between the two groups based on demographic characteristics demonstrated no significant differences. It concluded that no significant correlation between neonatal jaundice in term infants and the route of delivery. Karen E. Muchowski et al[6] reported that although neonatal jaundice is common, acute bilirubin encephalopathy and kernicterus (i.e., chronic bilirubin encephalopathy) are rare. Universal screening for neonatal hyperbilirubinemia is controversial. The American Academy of Paediatrics recommends universal screening with bilirubin levels or targeted screening based on risk factors. However, the U.S. Preventive Services Task Force and the American Academy of Family Physicians found insufficient evidence that screening improves outcomes. Universal screening may also increase rates of phototherapy, sometimes inappropriately. Younger gestational age and exclusive breastfeeding are the strongest risk factors for the development of hyperbilirubinemia. Infants who appear jaundiced should be evaluated by a risk score or by measurement of total serum or transcutaneous bilirubin. Phototherapy is an effective treatment for hyperbilirubinemia, but the number needed to treat varies widely depending on sex, gestational age and time since delivery. If indicated, phototherapy should be initiated based on gestational age and risk factors. Exchange transfusion leads to complications in about 5% of treated infants and has a mortality rate of three or four per 1,000 infants. Infants who breastfed exclusively particularly those who consume inadequate calories are at increased risk of hyperbilirubinemia. However, interrupting breastfeeding for the treatment of jaundice increases the risk of early discontinuation of breastfeeding. Encouragement from healthcare professionals is important to promote breastfeeding in these situations. Meredith L. Porter et al[7] reported that hyperbilirubinemia is one of the most common problems encountered in term newborns. Historically, management guidelines were derived from studies on bilirubin toxicity in infants with haemolytic disease. More recent recommendations support the use of less intensive therapy in healthy term newborns with jaundice. Phototherapy should be instituted when the total serum

bilirubin level is at or above 15 mg per dL (257 mol per L) in infants 25 to 48 hours old, 18 mg per dL (308 mol per L) in infants 49 to 72 hours old and 20 mg per dL (342 mol per L) in infants older than 72 hours. Few term newborns with hyperbilirubinemia have serious underlying pathology. Jaundice is considered pathologic, if it presents within the first 24 hours after birth. The total serum bilirubin level rises by more than 5 mg per dL (86 mol per L) per day or is higher than 17 mg per dL (290 mol per L), or an infant has signs and symptoms suggestive of serious illness. The management goals are to exclude pathologic causes of hyperbilirubinemia and initiate treatment to prevent bilirubin neurotoxicity. Thomas B. Newman et al[8] conducted a nested case control study using electronic and paper records, retrospective cohort study in Northern California Kaiser Permanente Hospitals. It was reported from the study that the risk index performed similarly in the validation group born in 1997-1998 and the derivation group born in 1995-1996 (area under the receiver operating characteristic curve = 0.83 vs. 0.84). Of the 5706 newborns with TSB levels measured before 48 hours, 270 (4.7%) developed a TSB level of 20 mg/dL or higher. Of these, 254 (94%) had a TSB level at the 75th percentile or higher at less than 48 hours. The risk index improved prediction over the TSB level alone, largely owing to the effect of gestational age. For example, for those with a TSB level at the 95th percentile or higher at less than 48 hours, the risk increased from 9% for newborns born at 40 weeks' or more gestation to 42% for those born at 36 weeks. This study concluded that clinical risk factors significantly improve prediction of subsequent hyperbilirubinemia compared with early TSB levels alone, especially in those with early TSB levels above the 75th percentile.

CONCLUSION

High cord bilirubin levels were associated to be in high-risk zone for later hyperbilirubinemia. Early bilirubin levels in healthy neonates were not associated to type of delivery or anaesthesia, late prematurity, feeding type and first meconium passage times.

REFERENCES

[1] Madlon-Kay DJ. Recognition of the presence and severity of newborn jaundice by parents, nurses, physicians, and icterometer. Pediatrics 1997; 100(3):eE3.
[2] Neonatal Jaundice: intensive care nursery house staff manual. UCSF Children's Hospital 2004:118-120.
[3] Garfunkel LC, Kaczorowski J, Christy C. Mosby's pediatric clinical advisor: instant diagnosis and treatment. Elsevier Health Sciences 2001: p. 200.
[4] Bilgin BS, Koroglu OA, Yalaz M, et al. Factors affecting bilirubin levels during first 48 hours of life in healthy infants. BioMed Research International 2013; 2013: 1-6.
[5] Farhat AS, Hafizi L, Pourhoseini MT, et al. Comparison of bilirubin level in term infants born by vaginal delivery and caesarean section. Iranian Journal of Neonatology 2016;7(4):45-49.
[6] Muchowski KE. Evaluation and treatment of neonatal hyperbilirubinemia. American Family Physician 2014;89(11):873-878.
[7] Porter ML, Dennis BL. Hyperbilirubinemia in the term newborn. Am Fam Physician 2002;65(4):599-606.
[8] Newman TB, Liljestrand P, Escobar GJ. Combining clinical risk factors with serum bilirubin levels to predict hyperbilirubinemia in newborns. Arch Pediatr Adolesc Med 2005;159(2):113-119.