

A Study of Factors Determining Idiopathic Hyperbilirubinemia in Healthy Term Neonates at MY Hospital, Indore, Madhya Pradesh

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Abstract: In our study total 402 healthy term newborns delivered in MYH Nursery were prospectively followed up and there Total Serum Bilirubin (TSB) levels on day 1, 3 & 5 were noted. 57 cases out of total 402 that is 14.2% developed significant Hyperbilirubinemia.

Keywords: Hyperbilirubinemia, Neonates, newborns, Total Serum Bilirubin

INTRODUCTION

Neonatal jaundice is very common condition seen upto 60percentage of newborns, in their first week of life. Unconjugated (indirect) hyperbilirubinemia occurs as a result of excessive bilirubin formation and inability of newborn liver to clear bilirubin rapidly enough from blood .One of the most prevalent clinical conditions is hyperbilirubinemia [1].

Out of total cases of neonatal jaundice, especially in the first week of life, nearly 8% to 11% of neonates develop significant hyperbilirubinemia. When the total serum bilirubin (TSB) rises above the 95th percentile for age (high-risk zone) during the first week of life, it will be considered as hyperbilirubinemia [2,3].

Around 60%–80% of healthy infants are expected to develop idiopathic neonatal jaundice [4]. Neonatal jaundice is the discoloration of skin and sclera color to yellowish in a newborn by bilirubin [5].

Therefore it can create concern in the physician and anxiety in the parents [6]. In neonates, the yellowish discoloration is first noted in the face and when the bilirubin level rises, it proceeds to the body and then to the extremities. This condition is common in 50%–60% of newborns in the first week of life [6]. Bilirubin is not merely a nuisance molecule that has dire consequences, but bilirubin such as uric acid is an important antioxidant circulating in biologic system of neonate [7–9]. However, high bilirubin levels can be toxic for central nervous system development and may cause behavioural and neurological impairment (Neurotoxicity or Kernicterus) even in term newborns [10-12]. Five to ten percent of newborns developed jaundice required the management of hyperbilirubinemia [13]. Neonatal jaundice may be on account of different parameters such as birth weight, gestational age, premature rupture of membranes, maternal infectious diseases or other illness during pregnancy, having different sources of origin, hence having different types [14]. The main causes of

increased bilirubin mostly are: race, genetic polymorphisms; inherited and acquired defects e.g. spherocytosis, Gilbert's syndrome, Najjar 1 and 2 Molecular genetics studies have shown the correlations between neonates hyperbilirubinemia and different genetic variations which can change in enzyme activity. Several types of Bilirubinaemia have been reported in neonates including physiological jaundice, pathological jaundice, jaundice due to breastfeeding or breast milk and hemolytic jaundice including three subtypes due to Rh factor incompatibility, ABO blood group incompatibility and Jaundice associated with Glucose-6-phosphate dehydrogenase (G6PD) deficiency [15].

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Glucose-6-phosphate dehydrogenase (G6PD) deficiency.

Physiological jaundice is the most common type of neonatal hyperbilirubinemia, having no serious consequences [16]. Neurodevelopmental abnormalities including as athetosis, loss of hearing, and in rare cases intellectual deficits, may be related to high toxic level of bilirubin [17]. Jaundice attributable to physiological immaturity which usually appears between 24–72 h of age and between 4th and -5th days can be considered as its peak in term neonates and in preterm at 7th day, it disappears by 10–14 days of life [18]. Unconjugated bilirubin is the predominant form and usually its serum level is less than 15 mg/dl [19]. Based on the recent recommendations of the AAP, bilirubin levels up to 17–18 mg/dl may be accepted as normal in term of healthy newborns [13].

Pathological jaundice is bilirubin levels higher from the normal range and requiring intervention [16]. Appearance of jaundice within 24 h due to increase in serum bilirubin beyond 5 mg/dl/day, peak levels higher than the expected normal range, presence of clinical jaundice more than 2 weeks and conjugated bilirubin (dark urine staining the clothes) would be categorized under this type of jaundice.

Babies on exclusive breastfeeding have a different physiological pattern for jaundice compared with artificially feed babies [15] and called Breast feeding jaundice. Jaundice in breast fed babies usually appears between 24–72 h of age, peaks by 5–15 days of life and disappears by the third week of life. Higher bilirubin levels have been reported in these infants [20]. In case of breastfed newborns, mild jaundice may take 10–14 days after birth or may reoccur during the breast feeding period [21]. Very large amounts of bilirubin rarely accumulate in the blood and cause cerebral lesions, a situation known as nuclear jaundice [22]. These cuts may be followed by hearing loss, mental retardation, and behavioral disorders. A mild clinical jaundice has been observed in one third of all breastfed babies in the third week of life, which may persist for 2 to 3 months after birth in a few babies [23]. Decreased frequency of breastfeeding is associated with exaggeration of physiological jaundice. One of the significant procedures to manage the jaundice in a term healthy baby is the mothers' encouragement to breastfeed their babies at least 10–12 times per day [24].

Hyperbilirubinemia is also associated with breast milk of mother in neonates known as breast milk jaundice [25]. About 2%–4% of exclusively breastfed babies have jaundice in excess of 10 mg/dl in the third week of life. These babies in the third week of life with bilirubin serum levels higher than 10mg/dl should be considered for prolonged jaundice [26]. A diagnosis of breast milk jaundice should be investigated if the

serum bilirubin is predominantly unconjugated, other causes of prolonged jaundice have been eliminated and the infant is in good health, vigorous and feeding well and gaining weight adequately [27]. Mothers should be advised to continue breastfeeding at more frequent intervals and bilirubin levels usually diminish gradually. Discontinuity of breastfeeding is not recommended unless levels exceed 20 mg/dl [28].

High risk factors for hyperbilirubinemia (prematurity, haemolytic conditions, maternal hypothyroidism etc.) are well known, but other factors vary in different settings. In this study we had assessed factors affecting idiopathic hyperbilirubinemia in M Y hospital Indore

AIMS & OBJECTIVES

To study factors affecting neonatal hyperbilirubinemia in healthy term newborns

MATERIALS & METHODS

This was a prospective study a prospective study conducted at "Maharaja Yashwant Rao Hospital Indore" between August 2008 and September 2009.

All newborns with fulfilling following criteria were included:

- Gestation >37 weeks (based on last menstrual period and neonatal assessment by expanded New Ballard score)
- Birth weight >2.500 kg (weighed on a electronic weighing scale, accurate up to 10 grams)
- Absence of major congenital malformations and
- Residing in Indore or a nearby place and whose parents agreed to come for follow-up.

All the infants (normal vaginal delivery) were discharged as per unit policy (after 24 to 72 hr). For sake of convenience infants born between 4 AM to 6 PM were included.

EXCLUSION CRITERIA

Babies were excluded if there was

- Rh incompatibility
- Positive direct Coomb test(DCT)
- Instrumental vaginal delivery (Forceps or Ventouse)
- Cephalhematoma or sings of bleeding
- Birth asphyxia sphyxia (Apgar < 5 at five minute) or required intubation > 4 minutes.
- Maternal History of (Antepartum haemorrhage, Pregnancy induced hypertension, primary rupture of membrane, Diabetes mellitus)
- Evidence of heolysis on perihierl smear,
- Sepsis (Blood culture positive)
- Significant illness requiring NICU admission for > 12 hr

- Serum bilirubin measurement was done initially on first 24+ 6 hrs of life & then repeated on third and fifth day of life

All infant with significant NNHB underwent

- Complete blood and differential with retic count
- PS typing (evidence of hemolysis)
- Blood culture
- Hepatic and renal function tests

Newborns with total serum bilirubin (TSB) >12mg/dl were defined as significant hyperbilirubinemia

Cases with significant hyperbilirubinemia were treated with Phototherapy or exchange transfusion if indicated.

Laboratory investigations were done in hospital pathology lab.

The critical total serum bilirubin (TSB) level on first 24+6 hrs of life S highest sensitivity was determined by using CHI-SQUARE TEST at various levels(ie 3, 4, 5).

Serum bilirubin estimation was done by Van Den Berg method to know total and direct reacting bilirubin. Serum bilirubin estimation 1st, 3rd and 5th day of life. A detailed investigation s done in all newborns in which serum bilirubin exceeded 12mg/dl.

A detailed antenatal, natal and postnatal history and thorough physical examination was noted in proforma .Cases were excluded if evidence of hemolysis or septicemia was found.

ANTENATAL HISTORY

- Parity of mother
- Jaundice in previous sibilings
- Maternal illness (Diabetes mellitus)
- Medication during pregnancy (OC pills in 1st trimester)
- Toxaemia of pregnancy.
- Blood group of mother

NATAL HISTORY

- Obstructive or Prolonged labour
- Mode of delivery
- Oxytocin induced labour
- Premature rupture of membrane (PROM)

POST-NATAL HISTORY

- Birth asphyxia, RDS
- APGAR score
- Gestation age
- Breast feeding
- Urine and stool frequency
- Day of appearance of jaundice
- History of dullness regurgitation of feeds

SERUM BILIRUBIN ESTIMATION

Sreum bilirubin was estimated by Malloy and Evelyn (1937) at post graduate Research Lab, Chacha Nehru Bal Chikitsalaya Awam Anusandhan Kendra, Indore (M.P.).

RESULTS

Total 467 babies were studied out of which 52 were lost to follow up. Out of remaining 415 cases 13 were ruled out (septicaemia and evidence of hemolysis on peripheral smear).Thus remaining 402 cases were studied. 57 out of 402 ie 14.2 percent developed significant hyperbilirubinemia (TSB> 12 gm %).

Table-01: shows the distribution of various factors among the enrolled neonates

Factors		Frequency	Percentage
Gender	Male	206	51.2
	female	196	48.7
Birth weight	2.5-3	217	53.9
	3.0- 3.5	132	32.8
	>3.5	53	13.1
Mode of delivery	Normal vaginal	368	91.5
	LSCS	34	8.5
Parity	primipara	215	53.5
	multipara	187	46.5

Table-02: The various factors like maternal and neonatal blood group, haemoglobin of the neonate, passage of meconium within 24 hours of delivery were found to be associated with development of NNHB

Factors		TCB <12(%)	TCB>12(%)	Chi square value	P value
Gender	Male	175	36	3.03	0.04
	Female	170	21		
Mode of delivery	NVD	321	47	7.082	<0.001
	LSCS	24	10		
Hb of newborn	<16	279(80.9)	30(52.6)	21.03	<0.000
	>16	66(19.1)	27(47.4)		
Feeding pattern	Exclusive BF	198(57.4)	39(68)	3.9	0.048
	Mixed feeding	110(31.9)	12(21.05)		
	Top feeding	37(10.7)	6(10.52)		
Parity	Primipara	183(53)	32(56.1)	0.18	0.33
	Multipara	162(47)	25(43.9)		
Meconium passed in 24 hours	Yes	121(35.1)	23(40.4)	0.59	0.22
	No	224(64.9)	34(59.6)		

As seen in the table the gender of the child, haemoglobin of newborn and mode of delivery were significantly associated with neonatal hyperbilirubinemia in healthy term neonates.

Table-03: Shows the association of neonatal and maternal blood group.

Factors		TCB <12(%)	TCB>12(%)	Chi square value	P value
neonatal blood group	A	125(36.2)	23(40.4)	0.58	0.89
	AB	12(3.5)	2(3.5)		
	B	94(27.2)	13(22.8)		
	O	114(33.0)	19(33.3)		
maternal blood group	A	149(43.2)	21(36.8)	1.2	0.75
	AB	22(6.4)	3(5.3)		
	B	79(22.9)	16(28.1)		
	O	95(27.5)	17(29.8)		

The association of neonatal and maternal blood group. No significant association is seen.

DISCUSSION

In this study, all the babies with neonatal jaundice were of term gestation. Out of 402 neonates studied, 51.2% were males and 48.7 were females. This matches earlier studies by Effiong *et al.*, Narang *et al.* and Korejo *et al.* where majority of the babies were males [29-31].

In our study majority of babies were between birth weight 2.5kg to 3kg (54%) followed by 3.0kg to 3.5kg (32.8%). Percentage of normal vaginal deliveries was high ie 91% and 54% mothers were primiparous. Significant hyperbilirunimia in our study was 14 percent ie 57 out of 402 neonates; this finding is consistent with the findings of the study conducted by Bhutani *et al.* [32] and Mishra *et al.* [15].

The incidence of significant hyperbilirubinemia depends on regional variations, ethnicity, of population and laboratory variability in measurement of bilirubin. These factors did not have a major consideration in our study.

Association of breast milk and neonatal jaundice is significant in our study and has been

reported significant in other studies as well [6, 11, 13]. Hence, Exclusive breastfeeding is a known risk factor hyperbilirubinemia.

In our study no association was seen between parity and hyperbilirubinemia, which is consistent with the findings of the study conducted by narang *et al.* [30].

There is no significant association between maternal and neonatal blood group as incompatibilities have already been excluded from our study.

CONCLUSION

All the maternal factors included in this study could not clearly predict the incidence of NNHB which continues to be a problem towards early discharge of normal newborn babies.

Gender, mode of delivery, Hb of neonate and exclusive breast feeding are associated with idiopathic hyperbilirubinemia. On the other hand, parity of mother, late passage of meconium, compatible blood group of mother and neonate – all these factors do not have any association with neonatal hyperbilirubinemia.

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