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Original Research Article

A Hospital-Based Observational Assessment of Pathological Jaundice in Late Preterm Neonates

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Abstract

Aim: The aim of the present study was to determine the incidence, progression and the predictors of pathological jaundice among the late preterm infants admitted in Paediatrics ward of a tertiary care centre

Material & Methods: A hospital based prospective cohort study was carried out in Department of Pediatrics for the period of two years, Sample size was 200 based on consecutive sampling.

Results: In the present study, 70% were male and 30% were female. Of them, 45%, 43% and 12% were 36, 35 and 34 gestational weeks respectively. Their mean birth weight was 2307.3 grams while the median birth weight was 2500 grams with a minimum of 1300 grams and a maximum of 3400 grams. Majority (42%) of the neonates were of B+ve blood group followed by A +ve (23%), while O +ve and AB +ve blood groups were noted in 20% and 15% respectively. Majority of the neonates (60%) were exclusively breast fed. 18.0% and 22% were formula fed and mixed fed respectively. Pathological jaundice developed among 68% neonates. Pathological jaundice was higher among the neonates who were delivered at 34 weeks of gestation when compared to others but it was not found to be statistically significant (p=0.105). Pathological jaundice was found to be higher among the neonates who were exclusively breast fed (76.66%) when compared to formula feeding (61.11%) and mixed feeding (50%) but it was found to be statistically significant (p=0.048).

Conclusion: Jaundice is condition that is often present and constitutes one of the major risks for neurodevelopmental issues in later life and the risk is further compounded by prematurity. Hence further studies with a larger sample size on a multicentric level could add robustness to our study thereby helping in better understanding and management of the condition.

Results: Late-preterm, Pathological jaundice, Total serum bilirubin, Exchange transfusion.

Introduction

Neonatal hyperbilirubinemia (NH) is a common problem that occurs in about 60% of newborns during the first week of life.[1] Neonatal jaundice (NNJ) is a yellow-orange discolouration of the skin and sclera of neonates because of excessive bilirubin in the skin and mucous membranes.[2] Bilirubin is a known antioxidant at low concentrations but a potent neurotoxin at high concentrations.[3] Hyperbilirubinaemia can be described in the form of pathological, physiological, jaundice secondary to breast milk or breastfeeding failure, and haemolytic jaundice due to glucose-6-phosphate dehydrogenase deficiency, ABO and Rh incompatibility.[4,5,6] . Pathological jaundice, on the other hand, develops during the first 24 h of life. [7] Jaundice can be severe when it is seen anywhere on the body on the first day or the hands and feet in addition to the arms and legs on the next Day.

The transition from progressive hyperbilirubinemia to acute bilirubin encephalopathy is often rapid and unpredictable because of a very narrow margin of safety. In newborns, jaundice appears when total bilirubin (TB) is more than 120 µmol/L.[8,9] Hyperbilirubinaemia with a TB 428–513 µmol/L is associated with an increased risk for bilirubin-induced neurological dysfunction with a significant risk of neonatal mortality and long-term neurodevelopmental sequelae. [10] Hyperbilirubinemia in preterm infants is more prevalent, severe, and protracted than in term infants due to the short life span of their red blood cells (RBCs), and the immaturity of their liver and gastrointestinal tracts. Often, there is also a delay in enteral feeding, which may limit intestinal motility and bacterial colonization, resulting in decreased clearance of bilirubin. These developmental and clinical phenomena contribute to the greater degree

and duration of neonatal hyperbilirubinemia in premature infants. [11] It can be managed by therapeutic interventions which include phototherapy, exchange transfusion and improving the frequency and efficacy of breast feeding or supplementing inadequate formula breast feeding. [6,8,12]

In Pathological jaundice, an elevation of TB that requires phototherapy, rate of rise in TSB or TcB level of >0.2 mg/dl/hour and jaundice persisting after 14 days in term and 21 days in late-preterm infants.[13] Significant jaundice may indicate underlying disease. High serum unconjugated free bilirubin is neurotoxic and can cause deafness, kernicterus, or athetoid cerebral palsy. The early identification of neonates who are at a greater risk of developing severe NNJ is of paramount importance to prevent brain damage.[14]

Therefore, this study aimed to identify the determinants of NNJ among neonates admitted at referral hospitals in Bihar region.

Material & Methods

A hospital based prospective cohort study in the Department of Pediatrics, N.M.C.H, Patna, Bihar, India for a period of two years Sample size was 200 assuming the prevalence as 10.1 from previous study conducted by Lavanya et al [15]

Study variables

Independent/predictor variables: These include age of the neonate in hours, gender of the neonate, birth weight in (kg), serum bilirubin, and age of onset of jaundice in hours.
Dependent/outcome variables: These include: proportion of neonates with pathological Jaundice, and association of pathological jaundice with independent predictors.

Inclusion Criteria

All consenting inborn late preterm neonates with postmenstrual age of 34 0/7 to 36 6/7 weeks were eligible for inclusion.

Exclusion Criteria

Late preterm neonate, discharged before 48 hours of life, and with major congenital malformations were excluded.

Study Procedure

After obtaining permission from the institute ethics committee and informed consent from the legal guardians of the neonates, a pre-designed proforma was used to collect the socio-demographic and the natal characteristics of the neonates. The neonates were followed up for the appearance of significant jaundice using necessary blood investigations. Relevant maternal, perinatal and neonatal variables were prospectively recorded. TSB was measured in all enrolled neonates at 0-12, 12-24, 25-36, 36-48 hours of life and when indicated clinically thereafter. Neonates were followed up during the hospital stay and after discharge till completion of the 14th postnatal day. The key outcome was significant hyperbilirubinemia defined as need of phototherapy on the basis of American academy of paediatrics guidelines.

Statistical Analysis

Data was entered in IBM statistical package for the social sciences (SPSS) statistics version 21 for windows (IBM Corp. 1995, 2012). For categorical variables: Chi-square test or Fisher's exact probability test was used and for continuous variable, analysis of variance (ANOVA) test was used.

Results

Table 1: Demography of the neonates studied

Gender	**N%**
Male	140 (70)
Female	60 (30)
Gestation (weeks)	
34	24 (12)
35	86 (43)
36	90 (45)
Blood group of the neonate	
O +ve	40 (20)
B +ve	84 (42)
A +ve	46 (23)
AB +ve	30 (15)
Birth weight	
LGA	4 (8)
AGA	180 (90)
SGA	6 (12)
Type of feed	
BF	120 (60)
FF	36 (18)

MF	44 (22)
Pathological jaundice	
Yes	136 (68)
No	64 (32)

In the present study, 70% were male and 30% were female. Of them, 45%, 43% and 12% were 36, 35 and 34 gestational weeks respectively. Their mean birth weight was 2307.3 grams while the median birth weight was 2500 grams with a minimum of 1300 grams and a maximum of 3400 grams. Majority (42%) of the neonates were of B+ve blood group followed by A +ve (23%), while O +ve and AB +ve blood groups were noted in 20% and 15% respectively. Majority of the neonates (60%) were exclusively breast fed. 18.0% and 22% were formula fed and mixed fed respectively. Pathological jaundice developed among 68% neonates.

Table 2: Association of period of gestation and type of feeding with pathological jaundice

Gestationalage (weeks)	Pathologic jaundice		P value
	Yes, n (%)	No, n (%)	
34	22 (91.66)	2 (8.34)	0.105
35	56 (65.11)	30 (34.88)	
36	58 (64.44)	32 (35.56)	
Type of feeding			
Breast feeding	92 (76.66)	28 (23.34)	0.048
Formula feeding	22 (61.11)	14 (38.89)	
Mixed feeding	22 (50)	22 (50)	

Pathological jaundice was higher among the neonates who were delivered at 34 weeks of gestation when compared to others but it was not found to be statistically significant (p=0.105). Pathological jaundice was found to be higher among the neonates who were exclusively breast fed (76.66%) when compared to formula feeding (61.11%) and mixed feeding (50%) but it was found to be statistically significant (p=0.048).

Table 3: Association of urine culture and sensitivity and sepsis screening and blood group with pathological jaundice

Parameters	Pathologic jaundice		P value
	Yes, n (%)	No, n (%)	
Urine culture and sensitivity			
Positive	16 (100)	0	0.046
Negative	120 (65.21)	64 (34.78)	
Sepsis screening			
Positive	40 (100.0)	0	<0.001
Negative	96 (66.66)	64 (44.44)	
Blood group of the neonate			
O +ve	12 (30)	28 (70)	0.001
B +ve	68 (80.95)	16 (19.05)	
A +ve	34 (73.91)	12 (26.09)	
AB +ve	22 (73.34)	8 (26.66)	

There was a significant association for positive urine culture and sensitivity and positive sepsis screening with pathological jaundice (p<0.05). Pathological jaundice was higher among the neonates with B +ve blood group when compared to others and it was found to be statistically significant (p=0.001).

Discussion

Jaundice is the visible manifestation in the skin due to elevated serum concentrations of bilirubin. Hyperbilirubinemia is the most common clinical condition requiring evaluation and treatment in the newborn and a frequent reason for hospital readmission during the first week of life. [16] Physiologic jaundice is very common in the first week of life which gradually subsides between 10-14 days of life. Jaundice in first week of life occurs approximately in 60% of term infants and 80% of preterm infants. [17] Although generally a benign, postnatal, transitional phenomenon in majority of the neonates, a few neonates develop marked potentially hazardous bilirubin levels that can pose a direct threat of serious brain injury. [18] Late preterm infants are those born at a gestational age of 34 0\7 to 36 6/7 weeks (239- 259 days deliveries during this late preterm period are increasing days. Deliveries since even mild prematurity is now recognized to be associated with adverse health outcomes, it poses healthcare challenges. They present with inadequate thermoregulation, immature and weak suck and swallow patterns,

incomplete adaptation of certain enzyme systems like decreased glucuronyl transferase enzyme activity, and a slower postnatal maturity of hepatic bilirubin uptake and poor immunological and respiratory systems.[19]

In the present study, 70% were male and 30% were female. Of them, 45%, 43% and 12% were 36, 35 and 34 gestational weeks respectively. Their mean birth weight was 2307.3 grams while the median birth weight was 2500 grams with a minimum of 1300 grams and a maximum of 3400 grams. Majority (42%) of the neonates were of B+ve blood group followed by A +ve (23%), while O +ve and AB +ve blood groups were noted in 20% and 15% respectively. Majority of the neonates (60%) were exclusively breast fed. 18.0% and 22% were formula fed and mixed fed respectively. Pathological jaundice developed among 68% neonates. Pathological jaundice was higher among the neonates who were delivered at 34 weeks of gestation when compared to others but it was not found to be statistically significant (p=0.105). Pathological jaundice was found to be higher among the neonates who were exclusively breast fed (76.66%) when compared to formula feeding (61.11%) and mixed feeding (50%) but it was found to be statistically significant (p=0.048). Due to relative deficiency of uridinedi phosphoglucuronate-glucuronosyl transferase there is more chance of hyperbilirubinaemia among late-preterm infants than term infants.[20] Also, late-preterm infants have increased chances of developing hyperbilirubinaemia because feeding difficulties that predispose them to an increase in enterohepatic circulation, decreased stool frequency, and dehydration.[21,22]

Of them, 45%, 43% and 12% were 36, 35 and 34 gestational weeks respectively. Mortality among infants less than 28 weeks was very high and hyperbilirubinemia contributed to 11% of all deaths of preterm babies. [23] Of the surviving preterm babies two-thirds developed hyperbilirubinemia. This finding is similar to the study done in India which found the highest prevalence among those less than 30 weeks.[24] Another two studies from India also showed that infants with low gestational ages (<37 weeks) were at higher risk of severe hyperbilirubinemia.[25,26] A study by Lavanya et al showed that large for gestation, gestational age, birth trauma and previous sibling with severe jaundice are the clinical variables significantly associated with significant jaundice.[27] Similar findings were reported by studies conducted by Keren et al, Bansal et al, Aziz et al and Knupfer et al, where lower gestation age (34 and 35 weeks), large for gestation age (LGA), ABO incompatibility and previous sibling with jaundice were significantly associated with significant hyperbilirubinemia.[28-31] There was a significant association for positive urine culture and sensitivity and positive sepsis screening with pathological jaundice ($p<0.05$). Pathological jaundice was higher among the neonates with B +ve blood group when compared to others and it was found to be statistically significant (p=0.001). In a study by Aynalem et al, Rh incompatibility (p=0.002), ABO incompatibility, perinatal asphyxia and sepsis were significantly associated with hyperbilirubinemia.[32]

Our study results have shown that male gender, breast feeding, , infants blood group (B +ve) among neonates were significantly associated with the development of neonatal hyperbilirubinemia. However, decreasing gestational age, birth weight, mode of delivery, abnormal thyroid and liver function tests and G6PD deficiency were not significantly associated.

Conclusion

Jaundice is condition that is often present and constitutes one of the major risks for neurodevelopmental issues in later life and the risk is further compounded by prematurity. Concern about neonatal hyperbilirubinemia is imperative, given the inherent risk of subsequent development of kernicterus. Late preterm neonates are usually treated and managed no differently from those of term neonates with respect to diagnosis, treatment and follow-up of hyperbilirubinemia. Over the years several studies had been conducted to determine the predictors of significant hyperbilirubinemia among the neonates. Hence further studies with a larger sample size on a multicentric level could add robustness to our study thereby helping in better understanding and management of the condition.

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