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Original Research Article

Factors identifying babies at risk for significant hyperbilirubinemia: a prospective study conducted at a tertiary care center

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ABSTRACT

Background: Hyperbilirubinemia is universally present in the newborn period and is recognized as clinical jaundice in approximately 50% infants. The aim was to determine the risk factors and treatment modalities of newborns with significant hyperbilirubinemia admitted from September 2011 to August 2013.
Methods: One hundred and fifty newborns with significant hyperbilirubinemia, both inborn and outborn were included in the study. Relevent information during hospitalisation was taken. American Academy of Pediatrics (AAP) guidelines were followed to determine the treatment modality. Treatment in the form of either phototherapy or exchange transfusion was given.
Results: Out of 150 patients 90 were males and 60 females. Higher values of serum bilirubin were found in the female babies and this difference was statistically significant. One hundred and thirty four babies had a birth weight of more than 2 kgs and 16 less than 2 kgs. The serum bilirubin levels were more in babies more than 2 kgs and this was statistically significant. Ninety one babies were delivered vaginally and 59 by LSCS. Higher serum bilirubin levels were found in those delivered vaginally with the difference being statistically significant .ABO blood group incompatibility was seen in 70 babies, 6 babies with Rh incompatibility. ABO incompatibility resulted in higher serum bilirubin levels with the difference being statistically significant. Ninety six babies had a gestation of more than 37weeks and higher bilirubin levels were found in this group as compared to lesser gestational age baby, the difference was statistically significant. Eighty five patients were admitted before 72 hours of life and 65 after that. Higher serum bilirubin levels were found in those admitted later with a statistically significant difference. The presence of antenatal risk factors (P = 0.4), parity of the mother (P = 0.178) were not found to play a major role in development of significant hyperbilirubinemia. Phototherapy was used as treatment modality in 137 patients, whereas 13 required exchange transfusion.
Conclusions: Significant hyperbilirubinemia was found to be more common in female babies, more than 37weeks of gestation, delivered vaginally, with birth weight of more than 2kgs, with ABO blood group incompatibility, admitted after 72hrs of life and with no identified antenatal risk factors. Most commonly used treatment modality found in these cases was phototherapy.

Keywords: AAP, Newborns, Phototherapy, Significant hyperbilirubinemia, Serum bilirubin

INTRODUCTION

Hyperbilirubinemia is universally present in the newborn period and is recognized as clinical jaundice in approximately 50% infants. The sheer prevalence of neonatal jaundice and periodic occurrence of bilirubin associated encephalopathy ensures sustained interest in this subject. The fear for the level of 20 mg/dl has given anxious moments to doctors and the relatives of the 'jaundiced infant'. To the pediatrician jaundice remains

the most common and perhaps the most vexing problem in the well-baby nursery. Jaundice is observed during the first week of life in ~ 60% of healthy term newborns and 80% of preterm newborns. Bilirubin production is 2-3 times higher in normal term newborns compared with adults. The colour in jaundice usually results from accumulation of unconjugated, nonpolar, lipid soluble, bilirubin pigment (indirect reacting) formed from hemoglobin by the action of heme oxygenase, biliverdin reductase and non-enzymatic reducing agents in the reticuloendothelial cells.[1]

While jaundice per se is not preventable nonetheless early detection of threatening bilirubin levels permit initiation of phototherapy and prevents higher risk and high cost exchange transfusion therapy or kernicterus. The American academy of pediatrics (AAP) recommends that newborns discharged before or within 48 hours should have a follow-up visit after 2-3 days to detect significant jaundice and other problems.[2]

This is not possible in our country due to limited follow up facilities. The concept of prediction of jaundice offers an attractive option to pick up babies at risk for neonatal hyperbilirubinemia. An association between bilirubin levels and subsequent risk of hyperbilirubinemia has been reported.[3,4] Infants who are clinically jaundiced in the first few days are more likely to develop hyperbilirubinemia.[5,6]

Risk stratification for significant hyperbilirubinemia (SHB) has been done by measuring bilirubin load (absolute levels or rate of rise of serum total bilirubin or transcutaneous bilirubin), bilirubin production (exhaled carbon monoxide) and identifying underlying clinical risk factors. Therefore, before neonates are discharged from birth hospital those at risk of developing high bilirubin levels need to be identified.[7]

The purpose of the study is to determine the risk factors associated with development of significant hyperbilirubinemia in newborns, so that we can keep a close follow up of babies who have the risk factors of developing significant hyperbilirubinemia in the future. Also the study is intended to determine the treatment modality for significant hyperbilirubinemia.

METHODS

Hospital based prospective study was undertaken after approval from the ethical committee. Over a period of 2 years from September 2011 to August 2013 of the total 1080 NICU admissions, in MGM Medical College, Aurangabad, 150 babies were included in the study according to the inclusion and exclusion criteria.

All newborns brought in NICU (inborn+outborn) with significant hyperbilirubinemia were taken as inclusion criteria.

Exclusion criteria

- Newborns having lethal congenital malformations
- Newborns with severe cardiorespiratory problems
- Newborns with stay less than 24 hours in NICU.

Methodology

- Significant hyperbilirubinemia was defined as need of phototherapy or exchange transfusion for treatment of hyperbilirubinemia. The decision to start phototherapy was made on the basis of the age of the baby in hours and total serum bilirubin levels. Informed written parental consent was taken before enrolling the baby into the study.
- In all newborns detailed history, gestational age assessment by new ballard score, systemic general examination with particular attention to the factors known to be associated with hyperbilirubinemia was carried out
- Serum bilirubin estimation was done using monoreagent "Jendrassic and Grof" method. Whole blood was taken in micro-capillary and centrifuged at the rate of 3000 rpm for 5 minutes. Bilirubin estimation was done spectrophotometrically using the wavelength (530-560 nm) and biochromatic wavelength used is 540nm (dimensions RxL Max, siemens production, USA)
- Single surface phototherapy (SSPT)/double surface phototherapy (DSPT) was administered using special blue compact fluorescent tubes (20W)
- Phototherapy was provided with babies lying supine in open bassinets, using overhead blue 4 lamps, fluorescent units placed 25cm above the baby, with covering of the eyes and genitals. Breast feeding was encouraged
- Phototherapy was discontinued when serum bilirubin level fell below 13 mg/dl
- Maternal and neonatal data were collected in predesigned and pretested proforma. Bilirubin values were plotted on previously published nomograms.[8] Statistical analysis was done using the software Texasoft WINKS SDA 7 version 7.0.6. For two group comparison,'t' test was used. When more than two groups were to be compared ANOVA was used.

RESULTS

One hundred and fifty newborns with significant hyperbilirubinemia were analyzed for this study. Out of the 150 patients 90 were males and 60 were females. Females (18.66) were having significantly higher serum bilirubin levels as compared to males (17.53) with a p value of 0.039. One hundred and thirty four babies had a birth weight of <2 kgs and 16 were >2 kgs. Babies weighing >2 kg (18.16) were having more bilirubin as compared to those weighing <2 kg (16.13) with a p-value of 0.013. ABO blood group incompatibility was seen in 70 babies as opposed to 6 babies with Rh incompatibility.

ABO (17.98) incompatibility resulted in higher serum bilirubin levels with the difference being statistically significant (P=0.026). Ninety one babies were delivered vaginally and 59 by LSCS. Normal delivery babies had higher bilirubin levels (18.33) then LSCS born (17.31) with p value of 0.04. Eighty five patients were admitted before 72hrs of life and 65 after that. Babies of age more than 72 hours had higher bilirubin (19.9) than those less than 72 hours of age (16.06) with a p value 0f 0.001. The presence of antenatal risk factors (P=0.4) and parity of the mother (P=0.178) didn't play any role in development of significant hyperbilirubinemia. Phototherapy 137 (13.66) was the commonest mode of treatment used compared to exchange transfusion 13 (23.29). Ninety six babies had a gestation of more than 37weeks and higher bilirubin levels were found in this group as compared to a lesser gestational age, the difference was statistically significant (P <0.05).

Table 1: Risk factors associated with significant hyperbilirubinemia.

Variables		Mean	Number	Percentage	P value
Birth weight	<2 kg	16.13	16	10.66	0.013
	>2 kg	18.16	134	89.33	
Sex	Male	17.53	90	60	0.039
	Female	18.66	60	40	
Blood group incompatibility	ABO	17.98	70	46.66	0.026
	Rh	15.21	6	4	
Type of delivery	LSCS	17.31	59	39.33	0.04
	NVD	18.33	91	60.66	
Antenatal risks	Present	17.82	58	38.66	0.692
	Absent	17.64	92	61.33	
Age on admission	<72 hours	16.06	85	56.66	0.001
	>72 hours	19.92	65	43.33	
Treatment given	Phototherapy	17.66	137	91.33	
	Exchange transfusion	23.29	13	8.6	

Table 2: Gestation versus serum bilirubin.

	Preterm <35	Late preterm 35-37	Term >37	P value
Mean	16.3	17.9	18.29	
Number	16	38	96	<0.05
Percentage	10.66	25.33	64	

DISCUSSION

Early discharge of healthy late preterm and full term neonates from hospital influenced an increase in hospital readmission rates due to hyperbilirubinemia and even the more serious reappearance of kernicterus.

The expert committee for severe neonatal hyperbilirubinemia and European society for pediatric research and AAP published detailed recommendations emphasizing the importance of universal, systematic assessment of the risk of severe hyperbilirubinemia, be implemented at all birthing facilities and coordinated with continuing ambulatory care. Therefore, the identification of newborn babies at risk of severe hyperbilirubinemia is still one of the most challenging problems for the neonatologist.[9]

Previous studies done by Najib et al and Kalakheti BK et al showed the incidence of significant hyperbilirubinemia to be 15% and 3.45% respectively.[10,11] In the present study incidence of significant hyperbilirubinemia was 13.88 %.

The pathogenesis of significant neonatal hyperbilirubinemia often is multifactorial; individual factors confer different levels of risk.[12]

Various studies have found a direct linear relation between greater birth weight and significant hyperbilirubinemia.[10,12-16] In the present study the mean birth weight of the babies who developed significant hyperbilirubinemia was 2.46 kg. Higher levels were found in babies having a birth weight of more than 2 kgs compared to those with birth weight less than 2 kgs. This difference was found to be statistically significant with a P-value of 0.013.

Male gender is a known risk factor for hyperbilirubinemia.[17] Similar results showing a higher incidence of significant hyperbilirubinemia in male babies as compared to female babies was found in various other studies.[10,16,18-22]

In the present study it was found that 90/150 (60%) of the affected babies were males and 60/150 (40%) were females. But when the mean values of serum bilirubin were compared female babies had higher bilirubin levels as compared to males and this difference was found to be statistically significant with a P value of 0.039.

Gestational age of newborns have a correlation with significant hyperbilirubinemia. In various studies conducted it was found that a higher incidence of significant hyperbilirubinemia was seen in babies with full term gestation of more than 38 weeks.[12,19-26]

In the present study, 54/150 (36%) babies had a gestation of less than 37 weeks and 96/150 (64%) were more than 37 weeks of gestation. When the mean serum bilirubin levels of the two groups was compared, it was found that higher bilirubin levels were found in babies with a gestation of more than 37 weeks, which was statistically significant with a P value of <0.05. ABO incompatibility was more commonly associated with the development of significant hyperbilirubinemia as compared to Rh incompatibility.[10,16,18,21,26,27] OA was more commonly associated than OB blood group with significant hyperbilirubinemia.[12,15]

In the present study it was found that ABO incompatibility played a major role in development of significant hyperbilirubinemia similar to previous studies. 70/150 (46.66%) babies had ABO incompatibility as compared to 6 babies (4%) who had Rh incompatibility. When their mean serum bilirubin levels were compared this difference was also found to be statistically significant with a P value of 0.026. Higher incidence of significant hyperbilirubinemia in vaginally delivered babies compared to those by caesarean delivery was seen in various studies.[10,15,22,23]

In the present study 91/150 (60.66%) newborns were delivered vaginally without any instrumentation and 59/150 (39.33%) newborns were extracted by LSCS. It was found that higher bilirubin levels were associated with babies delivered vaginally compared to those born by LSCS. This difference was found to be statistically significant with a P value of 0.04.

In the present study, when a comparison of bilirubin levels was made between babies who had antenatal risk factors to those who didn't, it was found that there was no significant difference between the two (P = 0.692). Neither parity of the mother played a major role in development of significant hyperbilirubinemia. It was found that 85/150 (56.66%) babies were admitted with significant jaundice before 72 hours of life whereas 65/150 (43.33%) babies were admitted after 72 hours of life. When the mean serum bilirubin levels of the two groups were compared it was found that babies who were admitted after 72 hours of life had greater bilirubin levels as compared to those admitted earlier. This difference was found to be statistically significant with a P value of <0.001. This was similar to previous studies.[10,15,21,23,28]

In the present study, 131/150 (87.33%) newborns with significant hyperbilirubinemia received double surface phototherapy as a treatment modality. 6/150 (4%) babies received single surface phototherapy. 13/150 (8.6%) babies required exchange transfusion along with phototherapy. Phototherapy as a treatment modality was more commonly employed as compared to exchange transfusion. But when the different types of phototherapy, like double surface v/s single surface were compared amongst them for effectiveness, there was no difference, which was statistically proven with a P value of 0.875.

CONCLUSION

Multiple risk factors are associated with development of significant hyperbilirubinemia. Female sex is found to be at a greater risk of developing higher serum bilirubin levels when compared to the male babies. Babies born out of full term gestation and a birth weight of more than 2 kgs have higher bilirubin levels compared to those born preterm and with a birth weight of less than 2 kgs. Babies delivered vaginally have higher serum bilirubin levels. Those with ABO blood group incompatibility have higher chances of developing significant hyperbilirubinemia. Babies brought to the hospital at a later age, after 72 hours of life, have higher serum bilirubin levels and higher chances of readmission. Antenatal risk factors did not play a major role in development of significant hyperbilirubinemia. Phototherapy was more commonly used as a treatment modality.

Thus, it was concluded that though an early follow up is essential to recognize the development of significant jaundice, if we recognize the above mentioned risk factors while the baby is in hospital, before discharge, a more meticulous follow up of these babies can be carried out to prevent development of significant hyperbilirubinemia.

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