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Research Article

RISK FACTORS OF NEONATES WITH INDIRECT HYPERBILIRUBINEMIA IN A TERTIARY CARE HOSPITAL

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ABSTRACT
The overall incidence of neonatal jaundice as reported by various Indian workers varies from 54.6% to 77%. Although most of jaundiced infants are otherwise perfectly healthy, they make us anxious because bilirubin is potentially toxic to the central nervous system and if the serum bilirubin levels are very high kernicterus can develop. Hyperbilirubinemia is one of the most common and one of the most vexing problems that occur in the neonate. The objective was to study risk factors and mode of treatment of neonatal indirect hyperbilirubinemia. A total of 120 hospitalized neonates delivered at the hospital as well as babies referred from peripheries of age between 0-28 days in 1 yr duration were included in this study. Study population comprised of neonates with jaundice (those with serum bilirubin more than 10 mg/dl). 35% were having idiopathic jaundice, followed by 30% physiological jaundice, 15% ABO incompatibility. Premature rupture of membrane was seen in 6 neonates of which 1 neonate had ABO incompatibility, 1 neonate had cephalhematoma, 1 had physiological hyperbilirubinemia and 3 neonates had septicaemia. Various maternal risk factors like PROM, prolonged labour, toxemia of pregnancy and oxytocin induction of labour were associated with neonatal hyperbilirubinemia. In addition, various fetal factors of which most important prematurity and other birth asphyxia were associated with neonatal hyperbilirubinemia.

Keywords: *Neonate, Hyperbilirubinemia, Kernicterus, Anti D Gamma Globulin, ABO Incompatibility, LBW Baby*

INTRODUCTION
Hyperbilirubinemia is one of the most common and one of the most vexing problems that occur in the neonate. Although most of jaundiced infants are otherwise perfectly healthy, they make us anxious because bilirubin is potentially toxic to the central nervous system and if the serum bilirubin levels are very high kernicterus (bilirubin encephalopathy) can develop (Avery *et al.*, 1999). Most adults are jaundiced when serum bilirubin levels exceeds 2mg%. Neonates however may not appear jaundiced until the serum bilirubin concentration exceeds 5 to 7 mg% (Taeush *et al.*, 2005). Jaundice is the commonest abnormal physical finding in the neonates (Anand *et al.*, 1978). The overall incidence of neonatal jaundice as reported by various Indian workers varies from 54.6% to 77% (Sharma *et al.*, 1994).
In term babies, physiological jaundice appears between 30-72hrs of age, maximum intensity of jaundice is seen on the fourth day, and jaundice disappears by 10th day of life. Serum bilirubin does not exceed 15mg%. Among preterm babies age of onset of physiological jaundice is similar to the term babies, the maximum intensity of jaundice is reached on the 5th-6th day and it may persists upto 14 days. Serum bilirubin may go upto 15mg% (Singh, 2004). Assessment of jaundice should be done in the natural light. The pulp of finger or thumb is pressed on baby's skin, preferably, over a bony part till it blanches and underlying skin is noted for yellow colour. Clinical jaundice manifests on face at 4-8mg%,upper trunk at 5-12mg%,lower trunk and thigh at 8-16mg%,arms and lower legs at 11-18mg%.In addition staining of soles and palms occur at serum bilirubin level more than 15mg% (Ramesh Agarwal *et al.*, 2002; Misra and Govil, 1994).
Overproduction of bilirubin combined with immature mechanisms for conjugation and enhanced enterohepatic circulation of bilirubin contribute to the absorption and development of jaundice, which in most infants, is mild enough to be considered physiological and non-toxic (Taeush *et al.*, 2005). Jaundice occurs when the liver cannot clear a sufficient amount of bilirubin from the plasma (Behrmann *et al.*,

1969). Yellowish discoloration of the skin is the result of accumulation of unconjugated non-polar lipid soluble indirect reacting bile pigment (Johnson *et al.*, 1998). Pathological jaundice is known to occur in 4-8% of newborn babies. The common causes include blood group incompatibilities, prematurity, sepsis, G6PD deficiency and majority being idiopathic. Other less common causes include polycythemia, cephalhematoma (Gathwala *et al.*, 1997; Lochmann *et al.*, 2004). Immature newborn brain is susceptible to toxicity from unconjugated bilirubin resulting in kernicterus or bilirubin induced brain damage (BIND) (Ramesh Agarwal *et al.*, 2002).

The criteria for intervention to control hyperbilirubinemia vary in different clinical situations. Phototherapy is a cheap, effective and safe method of management of neonatal hyperbilirubinemia. It is effective in treating hemolytic as well as non-hemolytic hyperbilirubinemia. Prophylactic phototherapy is indicated for infants weighing less than 1500 grams (serum bilirubin level less than 5mg %) (Misra *et al.*, 1994; Singhal, 1992). Exchange transfusion is an effective method of lowering seriously elevated bilirubin; early exchange transfusion reverses the transient bilirubin brain damage. Most of the exchange transfusions are required in hyperbilirubinemia associated with septicemia, hemolytic disease and prematurity. Neonatal hyperbilirubinemia is common and studies available are relatively less so with this background kept in mind the present study was planned which will further try to analyze risk factors related to neonatal hyperbilirubinemia.

Aims and Objectives

1. To study risk factors and mode of treatment of neonatal indirect hyperbilirubinemia.
2. To study causes for neonatal indirect hyperbilirubinemia.

MATERIALS AND METHODS

The present study was conducted on total 120 hospitalized neonates at Department of Pediatrics of Shree Vasantrao Naik Govt. Medical College and hospital, Yavatmal from, June 09 to May10. The babies delivered at the hospital as well as babies referred from peripheries of age between 0-28 days in 1 yr duration were included in this prospective study. All the neonates i.e. full term, preterm, healthy and sick neonates were included which comprised of neonates with jaundice (those with serum bilirubin more than 10 mg/dl) hospitalized in neonatal and pediatric units at V.N. Govt. Medical College and hospital during study period.

Inclusion Criteria

1) Neonates with jaundice delivered inside or outside the Institute, admitted in NICU and pediatric ward respectively during study period.
2) Neonates with serum bilirubin more than 10 mg/dl
3) Age group between 0-28 days.
4) Those who were willing to participate in the study.

Exclusion Criteria

1) Babies attending outpatient department only.
2) Babies who went discharge against medical advice.
3) Babies who not give consented to participate in the study.
4) Babies above 28 days of age.

Method: Jaundice was ascertained by clinical methods and was confirmed by biochemical methods. Standard proforma was used to record detailed history, clinical finding and investigations in each baby with hyperbilirubinemia. Each baby delivered at hospital was carefully observed from birth onwards in day light, for appearance of jaundice. In babies with dark complexion, digital pressure over fore head was used to detect the icterus. In addition, babies coming from peripheries were examined thoroughly clinically and detailed investigations were done to detect the cause of jaundice. Serum bilirubin estimation was done by Van den Bergh method. The babies who were having serum bilirubin 10 mg/dl or less were not included in the study. Only those having serum bilirubin more than 10 mg /dl were included in the study. Detailed antenatal, natal and postnatal history was taken. Thorough clinical examination of every baby was done and all the necessary investigations such as Hemoglobin percentage was calculated

by Sahli's method, peripheral smear, reticulocyte count, Serum bilirubin (total, direct, indirect), blood group and Rh typing of baby and mother, Coomb's test – direct and indirect, VDRL, TORCH titre, G-6-PD deficiency screening and T3 and T4 levels, X –ray chest as per necessity, Serum bilirubin level was repeated, whenever required were done as per requirement. Treatment for hyperbilirubinemia was carried out. Babies were treated according to need by phototherapy, drug therapy and exchange transfusion. Serum bilirubin levels were monitored from time to time. Detailed record of each case was kept as per proforma.

RESULTS AND DISCUSSION

Table 1: Distribution of neonates according to causes of neonatal indirect hyperbilirubinemia

Sr.No.	Causes	Number	Percentage
1	Idiopathic	42	35
2	Physiological	36	30
3	ABO incompatibility	18	15
4	Septicemia	12	8.34
5	Rh incompatibility	8	6.67
6	Cephalhematoma	4	3.33
7	G-6-P-D deficiency	1	0.83
8	Miscellaneous	1	0.83

Out of 120 neonates, the aetiology was idiopathic hyperbilirubinemia in 42(35%) neonates, physiological hyperbilirubinemia seen in 36 (30%) neonates, ABO incompatibility was a cause of hyperbilirubinemia in 17(14.16%) neonates, septicaemia in 10 (8.33%) neonates ,Rh incompatibility in 8 (6.66%) neonates, cephalhematoma in 3 (2.5%) neonates ,G-6-PD deficiency was a cause of hyperbilirubinemia in 1 (0.83) neonate ,and miscellaneous in 1 (0.83%) neonate, one neonate had both ABO incompatibility and septicemia, one neonate had both cephalhematoma as well as septicaemia.

Our findings are close to their findings. Merchant *et al.,* (1975) found idiopathic hyperbilirubinemia in 66% cases, Verma *et al.,* (1988) found idiopathic hyperbilirubinemia in 35% cases, Singhal *et al.,* (1992) found idiopathic hyperbilirubinemia in 34.4% cases while Narang *et al.,* (2001) found it in 57.8% cases. Our findings are close to that of Verma *et al.,* (1988) and Singhal *et al.,* (1992). Septicemia as cause of hyperbilirubinemia was found in 8% neonates by Merchant *et al.,* (1975), in 11.6% neonates by Verma *et al.,* (1988), in 5.7% neonates by Singhal *et al.,* (1992) and in 9.6% neonates by Narang *et al.,* (2001). Our findings are in accordance with that of Merchant *et al.,* (1975), Verma *et al.,* (1988) and Narang *et al.,* (2001). Rh incompatibility was found in 18.6% neonates by Merchant *et al.,* (1975), in 8.1% neonates by Singhal *et al.,* (1992), 2.9% by Narang *et al.,* (2001). In study by Verma *et al.,* (1988) 9.6% neonates had Rh incompatibility. Our findings are close to Verma *et al.,* (1988) and Singhal *et al.,* (1992). ABO incompatibility was found in 22.6% neonates by Merchant *et al.,* (1975), in 22.6% neonates by Verma *et al.,* (1988), in 14.3% neonates by Singhal *et al.,* (1992). Our findings are close to Singhal *et al.,* (1992). G-6-PD deficiency was found in 2.6% neonates by Merchant *et al.,* (1975), in 5.1% neonates by Singhal *et al.,* (1992) and in 3.4% neonates by Narang *et al.,* (2001). Our findings are closer to Merchant *et al.,* (1975). Cephalhematoma as a cause of jaundice was found in 2.6% neonates by Merchant *et al.,* (1975), in 2.9% neonates by Singhal *et al.,* (1992), in 6.3% neonates by Narang *et al.,* (2001). Our findings are matching with that of Singhal *et al.,* (1992). *Miscellaneous group* consisted of one neonate. The baby had many congenital anomalies in the form of contractures of knee and elbow joints, craniosynostosis, ambiguous genitalia, and bilateral Grade II hydronephrosis on ultrasonography of abdomen. The mother had history of previous two intrauterine deaths. This baby died on seventh day.

Table 2: Distribution of risk factors in neonatal indirect hyperbilirubinemia

Aetiology	No	Factors aggravating jaundice					
				Maternal		Fetal	
		PROM >18hrs	Toxemia	Prolonged Labour	Oxytocin induction	Prematurity	Birth asphyxia
Rh incompatibility	8	-	1	-	-	1	-
ABO incompatibility	18	1	-	1	-	3	1
Cephalhematoma	42	-	2	5	3	-	6
Idiopathic	4	1	-	2	1	-	-
Physiological	36	1	3	-	-	18	5
Septicemia	12	3	1	3	-	3	1
G-6-PD deficiency	1	-	-	-	-	-	-
Miscellaneous	1	-	-	-	-	1	-
Total		6	7	11	4	26	13

Maternal Factors

As shown in above table, premature rupture of membrane was seen in 6 neonates of which 1 neonate had ABO incompatibility, 1 neonate had cephalhematoma, 1 had physiological hyperbilirubinemia and 3 neonates had septicaemia.

Toxaemia of pregnancy was seen in 7 cases of which 1 had Rh incompatibility,2 had idiopathic jaundice,3 cases had physiological hyperbilirubinemia and 1 had septicaemia.

Prolonged labour was seen in 11 cases of which, 1 had ABO incompatibility,2 neonates had cephalhematoma,3 neonates had septicaemia and 5 neonates had idiopathic hyperbilirubinemia.

Oxytocin induction was done in 4 cases, out of which 3 had idiopathic hyperbilirubinemia and 1 neonate had cephalhematoma.

Fetal Factors

Prematurity was aggravating factor in 26 neonates of which 3 neonates had ABO incompatibility,3 neonates had septicaemia,1 neonate had Rh incompatibility,18 neonates had physiological hyperbilirubinemia and 1 neonate had various congenital anomalies.

One premature baby had both ABO incompatibility and septicaemia. One full term baby had both cephalhematoma and septicaemia.

13 neonates had birth asphyxia of which 1 neonate had ABO incompatibility,1 neonate had septicaemia and 6 neonates had idiopathic jaundice and 5 neonates had physiological hyperbilirubinemia.

Narang *et al.,* found oxytocin induction as a cause of hyperbilirubinemia in 2.4% cases. Singhal *et al.,* (1992), have found prematurity as a cause of jaundice in 16.7% of neonates. They have also found birth asphyxia as aggravating factor for hyperbilirubinemia in 12.1% cases out of which maximum were in idiopathic group. Our findings correlate with findings observed by Singhal *et al.,* (1992).

Table 3: Distribution of neonates according to mode of treatment therapy

Sr. No.	Mode of therapy	No.of patients	Percentage
1	Phototherapy alone	104	86.67
2	Exchange transfusion and phototherapy	16	13.33
3	Total	120	100

Of the total 120 neonates, 104 neonates were treated with phototherapy only and 16 neonates had to undergo exchange transfusion in spite of phototherapy.

Conclusion

1. Low birth weight babies formed major part of sample size. As maternal malnutrition is one of the important reasons for delivery of LBW baby; maternal nutrition prior to conception should be improved and maintained.

2. Anti D gamma globulin should be given to all Rh negative mothers whenever indicated.
3. Various maternal risk factors like PROM, prolonged labour, toxemia of pregnancy and oxytocin induction of labour were associated with neonatal hyperbilirubinemia. In addition, various fetal factors of which most important prematurity and other birth asphyxia were associated with neonatal hyperbilirubinemia.
4. Phototherapy is a cheap and effective way to reduce bilirubin levels in neonatal jaundice. It is also effective in lowering the bilirubin levels in hemolytic hyperbilirubinemia and thus reducing the need for exchange transfusion. The side effects associated with phototherapy are few and not serious.

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