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Research Article

PROFILE & CAUSES OF NEONATES WITH INDIRECT HYPERBILIRUBINEMIA IN A TERTIARY CARE CENTRE

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ABSTRACT
Hyperbilirubinemia is one of the most common and one of the most vexing problems that occur in the neonate. 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. The objective was to study profile of neonates and causes of neonatal indirect hyperbilirubinemia. A total of 120 hospitalised 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).
71(59.17%) were fullterm & 49(40.83%) were preterm neonate. 56.67% were male & 43.33% were female. Maximum number of neonates 37(30.84%) were between 2001 to 2500 gms. 35% were having idiopathic jaundice, followed by 30% physiological jaundice, 15% ABO incompatibility. As maternal malnutrition is one of the important reasons for delivery of LBW baby; maternal nutrition prior to conception should be improved and maintained. Anti D gamma globulin should be given to all Rh negative mothers whenever indicated.

Key Words: *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). 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).
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 10^{th} 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 5^{th}-6^{th} 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). 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 & studies available are relatively less so with this background kept in mind the present study was planned which will further try to analyse profile & causes related to neonatal hyperbilirubinemia.

Aims and Objectives

1. To study profile of neonatal indirect hyperbilirubinemia.
2. To study causes for neonatal indirect hyperbilirubinemia.

MATERIALS AND METHODS

The present study was conducted on total 120 hospitalised 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) hospitalised in neonatal & 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 & 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 gestational age

Sr. No.	Gestational age	Number	Percentage
1	More than 37 weeks (Fullterm)	71	59.17
2	28-30 weeks	21	17.5
3	31-32 weeks	20	16.66
4	33-36 weeks	08	6.66
	Total	120	100

Out of 120 neonates, 49 neonates were less than 37 weeks gestation and 71 neonates were having gestational age more than 37 weeks.
Out of 49 neonates with gestational age less than 37 weeks 21 (17.5%) were between 28-30 weeks gestation, 20 (16.66%) were between 30-32 weeks gestation and 08 (6.66 %) neonates had gestational age between 33-36 weeks.
Singhal *et al.,* (1992) have found prematurity as the second most common cause of hyperbilirubinemia in their studies. Prematurity was seen in 16.7% cases. Narang *et al.,* (2001) found jaundice in 440 (47.9%) out of 917 preterm babies.

Table 2: Sex wise distribution of neonates with hyperbilirubinemia

Sr. no.	Sex	Number	Percentage
1	Male	68	56.67
2	Female	52	43.33
	Total	120	100

120 neonates were studied, of which 68 (56.67%) were male and 52 (43.33%) were females. These results are consistent with results of other studies. Narang *et al.,* (2001) have also found a male predominance in their studies with 56.2% cases of male sex.
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. In studies by Merchant *et al.,* (1975), physiological jaundice was seen in 25.3% cases.

Table 3: 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

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 4: Distribution of neonates depending upon birth weight

Sr. No.	Weight (grams)	Number	Percentage
1	1000-1500	14	11.67
2	1501-2000	29	24.16
3	2001-2500	37	30.84
4	2501-3000	29	24.16
5	>3000	11	9.17
	Total	120	100

In the study of 120 neonates, 14 (11.67%) neonates were between 1000gm to 1500 gm while 29 (24.16%) neonates were between 1501 to 2000 gm. Maximum number of neonates i.e. 37 (30.84%) were between 2001 to 2500 gm, 29 (24.16%) neonates were between 2501 to 3000 gm and 11(9.17%) neonates were above 3000 gm weight.

Most of the neonates i.e. 80 were less than 2.5 kg i.e. with low birth weight. Singhal *et al.*, (1992) found in his study that one fourth of neonates (29.16%) developing hyperbilirubinemia was with low birth weight.

Narang *et al.*, (2001) concluded from their studies that the incidence of neonatal jaundice was three times higher in LBW babies compared to babies above 2500 g.

In our study 66.66% neonates were low birth weight, it is mainly because of maternal undernutrition, poverty, under utilization of health services and illiteracy seen in this rural area.

Table 5: Distribution of neonates according to serum bilirubin level

Sr.No.	Serum bilirubin level (mg/dl)	Number	Percentage
1	11-15	38	31.67
2	15.1-18	46	38.33
3	18.1-20	21	17.50
4	>20	15	12.50
	Total	120	100

In present study 38 (31.67%) neonates were having serum bilirubin level between 11-15mg/dl, 46 (38.33%) neonates had serum bilirubin between 15.1-18 mg% 21 (17.50%) neonate's serum bilirubin was between 18.1-20 mg/dl and in 15 (12.5%) neonates it was more than 20mg/dl.

The peak serum bilirubin levels achieved due to various causes as studied by Singhal *et al.*, (1992) are idiopathic 16.9±4.1mg/dl, in septicemia 17.6±4.1mg/dl, in Rh isoimmunisation 22.7±4.6mg/dl and in cephalhematoma as 17.8±4.3 mg/dl. Narang *et al.*, (2001) found total serum bilirubin level as less than 15mg/dl in 51.8% cases and more than 15mg/dl in 48.2% cases. Our findings are matching with that of Singhal *et al.*, (1992).

Table 6: Distribution of neonates according to type of delivery

Sr. No.	Mode of delivery	Number	Percentage
1	Vaginal	91	75.83
2	Caesarean section	25	20.84
3	Breech	04	03.33
	Total	120	100

Out of 120 neonates, 91 (75.83%) neonates were born by vaginal delivery, 25(20.84%) neonates were born by Caesarean section and 4(3.33%) neonates were born by breech delivery.

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. Blood group of all the neonates, born to mothers having 'O' blood group and/or Rh 'negative' type should be checked at birth. This will help to determine high risk neonate, who can be frequently examined before discharge.

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