

# NEONATAL HYPERBILIRUBINAEMIA

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PAEDIATRICIANS WILL GENERALLY agree there is a high incidence of jaundice among newborn infants in this country. Although several extensive studies have been carried out in Singapore (Wong, 1964 & 1966), there have been no reports concerning the incidence of neonatal hyperbilirubinaemia and the underlying factors responsible for the high serum bilirubin levels in Malaya.

This study was undertaken in an effort to widen our present knowledge on the incidence and aetiology of neonatal hyperbilirubinaemia.

## MATERIAL AND METHOD

The present study is based on observations made on 3,402 live-born infants who were delivered in the Maternity Unit, University Hospital, Kuala Lumpur, during the period January 1969 to June 1970. The infants (1,688 males and 1,714 females) comprised 1,851 Chinese, 759 Indians, 669 Malays and 123 of other races. They were the result of normal delivery in 2,710 cases, forceps delivery in 370, vacuum extraction in 59, breech delivery in 114 and Caesarean section in 149 cases respectively.

All newborn infants had estimation of cord erythrocytic glucose-6-phosphate dehydrogenase done routinely while ABO, Rhesus blood group typing and Direct Coomb's test were done in all mothers and infants.

All infants who developed jaundice whilst in hos-

pital were closely observed and were only discharged when the jaundice showed signs of abating. Infants who developed moderate or more than moderate jaundice were kept under surveillance and had repeated estimations of serum bilirubin until such time when the peak bilirubin level was passed. Exchange transfusion was carried out in cases where the serum indirect bilirubin level exceeded 20 mgs/100 ml. Cases of Rhesus incompatibility had exchange transfusions much earlier for obvious reasons.

All well babies were generally discharged by the fifth day after birth. Those found to have G-6-P.D. deficiency were kept in hospital for at least ten days, and on discharge mothers were instructed to report back with the infant at the earliest suspicion of jaundice.

Serum bilirubin levels were estimated using the method described by Malloy and Evelyn, erythrocytic glucose-6-phosphate dehydrogenase was determined using the method described by Prankerd (1962). (Normal values for G-6-P.D. obtained by this method do not usually exceed 90 minutes, intermediate values fall in the range between 120–150 minutes; while values exceeding 150 minutes definitely indicate deficiency. Personal communication — Dr. J.C. White.)

All cases of neonatal hyperbilirubinaemia encountered in the present study were classified under the following aetiological groups:—

Table 1: Aetiology of Hyperbilirubinaemia in the Different Ethnic Groups in the Present Study and in Singapore.

Cause	Chinese (36)	Indian (9)	Malay (5)	% of total cases	% Singapore cases (Wong 1966)
Idiopathic ("Liver Immaturity")	15	1	3	38	25
ABO incompatibility	9	3	—	24	16
G-6-P.D. deficiency	8	—	—	16	43
Prematurity	3	—	—	6	6
Rhesus incompatibility	—	4	—	8	2
Sepsis	1	—	2	6	8
Respiratory distress syndrome	—	1	—	2	—

**Rhesus incompatibility:** The diagnosis was only made if the infant was Rhesus positive, the mother Rhesus negative and the Direct Coomb's test positive.

**ABO incompatibility:** This was limited to A or B infants of blood group O mothers. Specific tests to demonstrate antibody in infants and mothers' sera were not undertaken.

**G-6-P.D. deficiency:** This embraces infants with abnormal G-6-P.D. values in cord blood. (This includes deficiency and intermediate values.)

**Prematurity:** This includes patients whose birth weight was less than 5 lbs and in whom there was no other apparent cause to account for the jaundice.

**Respiratory distress syndrome:** This embraces infants with idiopathic respiratory distress syndrome who developed jaundice during the course of their illness and in whom no other cause was found to account for the jaundice.

**Sepsis:** This includes patients with septicaemia, umbilical, urinary tract or severe skin infections and no other cause to account for the high bilirubin levels.

**Idiopathic:** This embraces infants whose birth weight was over 5 lbs and in whom no other cause was found to account for the hyperbilirubinaemia.

## RESULTS

### Incidence of Neonatal Hyperbilirubinaemia

From observations made on 3,402 newborn infants during their stay in hospital, it was found that 50 infants developed jaundice severe enough to warrant exchange transfusion.

### Type of Delivery

Of the 50 cases of neonatal hyperbilirubinaemia encountered in this study, 36 were the result of normal delivery. Chi-squared analysis was carried out to determine if there is a significant association between the type of delivery in these cases and the incidence of hyperbilirubinaemia.  $X^2$  was found to be 1.8377, and at one degree of freedom  $0.2 > P > 0.1$ . This is not significant. Thus it was concluded that there is no significant relationship between the incidence of hyperbilirubinaemia and the type of delivery.

### Sex

There were 31 males and 19 females in the present series. Chi-squared analysis was carried out to determine if there was an association between the sex of the infants and the incidence of hyperbilirubinaemia. The value of  $X^2 = 3.1429$  and at one degree of freedom is not significant as  $0.10 > P > 0.05$ . Thus there is no significant association between the sex of the infants and the incidence of neonatal hyperbilirubinaemia.

### Ethnic group

The 50 cases in the present series comprised 36 Chinese, 9 Indians and 5 Malays. Chi-squared analysis was carried out to determine if there was an associa-

tion between the ethnic group of infants, and the incidence of hyperbilirubinaemia.  $X^2$  was found to be 7.6764 and at 3 degrees of freedom  $0.10 > P > 0.05$ . It is thus apparent that there is no significant relationship between the ethnic origin of infants born in this hospital and the incidence of hyperbilirubinaemia.

#### Aetiology of Neonatal Hyperbilirubinaemia

Table I. summarises the incidence of the various causes of neonatal hyperbilirubinaemia in the different ethnic groups. ABO incompatible pregnancies accounted for 24 per cent of cases, G-6-P.D. deficiency for 16 per cent, Rhesus incompatibility for 8 per cent, prematurity for 6 per cent, sepsis for 6 per cent and respiratory distress syndrome for 2 per cent of cases respectively. The cause of jaundice was not established in 38 per cent of cases.

#### Exchange Transfusion

A total of 84 exchange transfusions were carried out in the 50 cases of hyperbilirubinaemia studied in 50 cases of hyperbilirubinaemia studied in the present series. No serious complications were encountered during these procedures apart from bradycardia and extra systoles which occurred in one case while another developed septicaemia a few days after exchange transfusion. There were no fatalities. Kernicterus did not occur in any of the cases observed in hospital except one who was taken home by the mother on the third day and was subsequently readmitted on the sixth day with severe jaundice and kernicterus. This infant had G-6-P.D. deficiency in addition to umbilical sepsis and prematurity. The fact that kernicterus did not occur in any of the babies observed in hospital is probably a reflection of the close vigil which was maintained and the timely use of exchange transfusions in preventing this complication.

#### DISCUSSION

There is a high incidence of hyperbilirubinaemia amongst newborn of Chinese, Indian and Malay origin. Approximately 1 in 70 babies delivered in this hospital required exchange transfusion. Although not statistically significant, the incidence appears to be higher in Chinese than in the other two ethnic groups. Approximately 1 in 50 Chinese, 1 in 80 Indian and 1 in 130 Malay newborn developed severe hyperbilirubinaemia.

The cause of hyperbilirubinaemia was established in 62 per cent of cases. The 2 commonest causes were ABO incompatibility and G-6-P.D. deficiency which together accounted for 40 per cent of cases. Sepsis, prematurity, Rhesus incompatibility and idiopathic

respiratory distress syndrome accounted for 22 per cent of cases. Rhesus incompatibility is relatively infrequent compared with the high incidence in Western countries. In the present series, Rhesus incompatibility accounted for 8 per cent of cases and occurred exclusively among those of Indian origin. This is not surprising as the Rhesus negative rate, amongst the 10,798 patients who attended the ante-natal clinics in this hospital, was 0.1 per cent in Chinese, 0.2 per cent in Malays, and 0.8 per cent in Indians as opposed to 15 per cent in Europeans (personal communication — Mr. G. Rajendran). Amongst the 4 cases of Rhesus incompatibility studied in the present series was one case which was salvaged by intra-uterine intra-peritoneal transfusion and multiple exchange transfusions following delivery. It is the first case of its kind to be salvaged by this method in Malaya.

G-6-P.D. deficiency is present in approximately 2 per cent of local Malays and Chinese, and in 0.2 per cent Indians (personal communication — Professor K.S. Lau). In the present series, hyperbilirubinaemia due to G-6-P.D. deficiency occurred only in Chinese infants. The reason for this is not clear.

On comparing the aetiology of hyperbilirubinaemia in babies born in University Hospital with that of babies born in Singapore (see Table I), it is seen that there is a higher incidence of hyperbilirubinaemia due to G-6-P.D. deficiency in Singapore. This can partly be accounted for by the marked predominance of Chinese in their population, as compared to that in Malaya. Approximately 22 per cent of babies born in this hospital are of Indian origin, and this has probably contributed towards the relatively lower overall incidence of hyperbilirubinaemia due to G-6-P.D. deficiency in the present series.

It is seen from Table I that the cause of jaundice was not found in 38 per cent of cases. Wong (1966) has attributed the cause of jaundice in such cases to "liver immaturity", where there is a transient depression of hepatic glucuronyl transferase activity in the immediate neonatal period resulting in failure of conjugation. Brown and Boon (1965) found that jaundice occurred in approximately 90 per cent of Chinese infants, 30 per cent of European infants and 70 per cent of Malay infants who were born in Singapore. They studied a large number of environmental factors but were unable to conclude that any were responsible for the ethnic group differences. Genetic cause for liver immaturity was excluded because the 3 racial groups behaved similarly in contradistinction to British infants and it was considered unlikely that the

3 different ethnic groups possess the same genetic abnormality.

There have been some recent reports on pyruvate kinase deficiency in Hongkong Chinese. It is not unlikely that this deficiency is present in a proportion of our local Chinese population. It is quite obvious that more detailed research has to be undertaken to elucidate the aetiology of hyperbilirubinaemia in patients in whom the cause of the jaundice has been ascribed to "liver immaturity" or idiopathic hyperbilirubinaemia.

#### SUMMARY

Observations were carried out on 3,402 infants who were born in the Maternity Unit of the University Hospital, Kuala Lumpur, during the period January 1969 to June 1970. Of these, approximately 1 in 50 Chinese, 1 in 80 Indian and 1 in 130 Malay newborn developed jaundice severe enough to require exchange transfusion.

The common causes of hyperbilirubinaemia were ABO incompatible pregnancies and G-6-P.D. deficiency. The other less common causes were Rhesus incompatibility, prematurity and sepsis. The cause of jaundice was not established in 38 per cent of cases.

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#### REFERENCES

1. Brown, W.R. & Boon, W.H. (1965) Ethnic group differences in plasma bilirubin levels of full-term healthy Singapore newborns. *Pediatrics*, **36**: 745.
2. Pranker, T.A.S. (1962) Broad sheet No. 42 (New Series). *Assoc. Clin. Pathologists*, October.
3. Wong, H.B. (1964) Neonatal hyperbilirubinaemia. *Bull. Kandang Kerbau Hosp.*, Singapore, **3**: 1.
4. Wong, H.B. (1966) Singapore kernicterus: A review and the present position. *Bull. Kandang Kerbau Hosp.*, Singapore, **5** (2): 1.

(Personal communications:

Dr. Lau, K.S. — Department of Pathology, University of Malaya.

Dr. White, J.C. — Department of Pathology, University of Malaya.

Mr. G. Rajendran — Blood Bank, University Hospital, Kuala Lumpur.)