

# A Newborn with Intravascular Haemolysis and Jaundice

## A Case of Haemolytic Disease of Newborn

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A case of Haemolytic disease of the newborn was presented by the Department of Obstetrics & Gynaecology and Paediatrics on 20-11-86.

Fateh Bibi a 35 years old house wife from Sargodha (Gravida-8, Para-7) was admitted on 25-9-86 through OPD with history of gestational amenorrhea of 30 weeks, and a poor obstetric history.

She had four macerated intra-uterine deaths; 2 were males and 2 were females. All were full term pregnancies and home deliveries. Last intra-uterine death occurred 3 years ago.

Past medical history and family history were essentially irrelevant. Her menstrual cycle was normal and regular. Her blood group, unknown to her, was A-ve and her husband was O+ve. She had never received Anti D injection in the past. Initial investigations revealed a healthy foetus of 28 week maturity. Antibody titer was 1:2; indirect coombs test was positive. Her fasting and post prandial blood sugar levels were within normal range. So GTT was not done. Blood Urea level, serum creatinine, Hb. Urine analysis were normal. She was given prophylactic anti-D injection on 3-10-86. She returned on 29.10.86 at 34 weeks of gestation when her antibody titer was repeated. It was 1:28 in the saline phase and 1:32 in the albumin phase.

Indirect Coomb's test was positive and the rest of the investigations were normal. Her Cardiocography was done, fetal cardiac activity (FCA) observed. No abnormality was detected. Since the prediction of the severity of Rh disease is 60% accurate with history and antibody titers, amniocentesis was planned, which is 95% effective in predicting and evaluating the severity of haemolytic disease of the newborn. Amniocentesis can be done as early as 22 weeks of pregnancy. The objective is to determine the level of bilirubin and bilirubinoid substances in the amniotic fluid. Their concentration reflects the degree to which the baby is affected with the haemolytic disease.

First ultrasonography was done. Placenta was in the upper uterine segment, posteriorly and the presenting part was the head. FCA was normal and no fetal abnormality seen. The procedure was started after evacuating the urinary bladder so as to avoid puncturing the urinary bladder. Under complete aseptic conditions in the operation theatre, local anaesthetic was administered in the suprapubic region. The presenting part was elevated, lumbar puncture needle of 20 gauge introduced. 10.0 ml of amniotic fluid was aspirated from the free pool of liquor amnii and sent for spectrophotometric study in a dark colored container to avoid light absorption. The complications with this procedure are maternal infection, placental injury, fetal injury and even premature induction of labour.

Liley in 1963 reported that there were at least seven bilirubinoid pigments which contributed to the absorption peak at 450 mus. The optical density of the liquor is plotted on semi logarithmic paper against a range of wave lengths ranging from 350 mus to 700 mus. The interest is concentrated on 450 mus range. For any given period of gestation, the height of the spectrophotometric bulge at 450 mus falls within one of the three well known Liley Zones.

### Zone-I:

Also known as the Lowest Zone - Baby is either unaffected or only mildly affected. Such babies are delivered at the term Amniocentesis 2-3 weeks later is repeated.

### Zone-II:

Intermediate zone is, again divided in 2 zones:-

#### (i) Lower Part:

Mild to moderately affected baby.

#### (ii) Upper Part:

Intrauterine blood transfusion is given before 34 weeks of gestation or early delivery after 34 weeks.

*Zone-III: Highest Zone:*

Baby is severely affected and intra-uterine death is imminent. Immediate delivery at or beyond 34 weeks of gestation is done after arranging Rh. negative blood transfusion in co-ordination with the Paediatric Department.

The report in this patient showed the peak in Zone-III. Immediate delivery of baby was decided as any further delay would have resulted in intra-uterine death. The fetus was of 35 weeks gestation at this moment. Our patient was induced medically on 11 November. The progress of labor was not satisfactory and fetal distress appeared. A lower segment Caesarian section was done in the early hours of 12th November, 1986 and a healthy baby girl with APGAR score 8/10 was delivered. The Paediatricians now took over the baby's care.

DR. MUHAMMAD AKBAR (*Medical Officer Paediatrics*) We were informed about this case, so all necessary arrangements for immediate exchange transfusion were made.

On 12 Nov. 86 at 2.00 A.M. a female newborn weighing 2.8 Kg of 35 weeks gestational age was delivered by L.S.C.S.. The baby was mildly jaundiced, colour was pink. Apgar score was 8/10 at 1 min. and 10/10 at 5 min. of age. Liver was palpable 2 cm below right costal margin whereas the spleen was just palpable. No other abnormality was found on physical examination. As there was no evidence of severity or hydrops fetalis, immediate exchange transfusion was postponed. Cord blood was sent to the laboratory and baby was shifted to the nursery. Her Bilirubin was monitored 4 hourly for the first 24 hours.

The cord blood showed a total S. Bilirubin of 5.8 mg (conjugated 2.6. mg), HB 16.5 Gm%, WBC  $8 \times 10^9/L$ , L-60% N-40% Retic Count 3.5% Platelets 21700. Direct coombs test +ve and indirect -ve.

Four hour monitoring of S. Bilirubin showed that it remained within safe limits except at the age of 48 hours. After 48 hours it had risen to 16.2 Mg/dl whereas haemoglobin had fallen to 8 Gm%.

Now a decision to do immediate exchange transfusion was made. Double volume exchange transfusion was done with O-ve blood. A newborn possesses 85 ml blood per Kg of body weight. So exchange transfusion was done with 480 ml of blood.

Stomach was aspirated through N/G tube to avoid vomiting and aspiration. Under strict aseptic measures the umbilical vein was catheterized. The catheter was pushed slowly into the inferior vena cava and central venous

pressure was estimated. Body temperature was maintained. Heart rate, respiration rate remained within limits throughout this procedure. Exchange was done in 20 ml aliquots. One ml of calcium gluconate and sodium bicarbonate were given after every 100 ml of exchange alternatively. The exchange was completed in 75 minutes. Samples for post exchange S. Bilirubin, Hb were drawn.

The two-volume exchange removes 80% of the affected RBCs. Post exchange S. Bilirubin was also carefully monitored which showed progressive fall in serum bilirubin except four hours after the exchange transfusion. At that time it was 15 Mg/dl which was considered as reactive hyperbilirubinemia. This occurs because extravascular S. Bilirubin is extracted back into the vascular system as free albumin is available to combine with it. Bilirubin was 8.3 Mg/dl 72 hours after exchange transfusion. Blue light phototherapy for 4 hours with 2 hours rest was given throughout this time period. Eyes were covered to decrease the side effects of phototherapy. No side effect due to exchange transfusion or phototherapy occurred in this patient. At present the baby is active, healthy looking. She is taking 60 ml of formula two hourly. H.R. = 138/Min. Chest is clear. Temperature 98 F<sup>0</sup> R.R. = 33/Min. Liver is one finger palpable whereas spleen is not palpable. She had a HB% 12.5 Gm and S. Bilirubin 6.5 Mg/dl.

In summary, this was an Rh positive baby born to an Rh-ve mother, a case of haemolytic disease in newborn due to Rh-incompatibility who required exchange transfusion at the age of 48 hours and now has improved. Today she will be sent home.

**Pathophysiology of Rh-incompatibility**

An Rh-ve mother bears an Rh+ve fetus. Fetal RBCs leak into the maternal circulation. Mother is naturally sensitized to causes her to produce immunoglobins of IgG variety. These cross the placenta, attach to fetal RBCs and cause their destruction resulting in haemolytic disease of the newborn. Small leaks of fetal RBC into maternal circulation occurs during whole of pregnancy but the major part occurs during labour or pregnancy in the fallopian tube or during abortion.

50% of the cases of Rh-incompatibility are mildly affected. In these HB% is normal and cord serum bilirubin is less than 5 mg/dl. These patients require no treatment but only close observation. A few patients like ours may require exchange transfusion at the age of 48 to 72 hours to avoid kernicterus.

25% of the cases are moderately affected. The newborn is severely jaundiced with marked hepatosplenomegaly. HB is below 10 Gm% and serum bilirubin of cord blood

is more than 5 mg/dl. These patients require immediate exchange transfusion with whole blood, cross matched to babies's group but Rh negative.

25% of the cases are severely affected and the newborn has either hydrops fetalis or is dead in utero. In these cases there is no time for cross matching and immediate exchange transfusion with O-ve blood group is indicated.

The 2nd important cause of haemolytic disease of newborn is ABO incompatibility. ABO incompatibility is more frequent but less severe than Rh-incompatibility. 12% of ABO incompatible couples are affected but only 5% show a positive Coomb's test and 1% require exchange transfusion. Frequency in first and subsequent pregnancies is the same.

### CAUSES OF HAEMOLYTIC DISEASE IN NEWBORN

These can be broadly classified into two broad groups.

1. RBC DISORDERS
2. IMMUNE MECHANISM

#### I. RBC Disorders

RBC Disorders are hereditary and acquired:—

- (a) Hereditary Defects:
  - (1) Membrane Defects
    - Hereditary spherocytosis
    - Hereditary elliptocytosis
  - (2) Enzyme Defects:
    - G 6 PD Deficiency and pyruvate kinase deficiency.
  - (3) Haemoglobinopathies:
    - Alpha, Beta and Theta Thalassemia Syndromes.
- (b) Acquired RBC Disorders:
  - (1) Disseminated & localized intravascular coagulation.
  - (2) Respiratory distress syndrome
  - (3) E. Coli and streptococcal septicaemia.

#### II. Immune Mechanism

- (i) RH, ABO and minor blood group incompatibility
- (ii) Immune diseases of mother like Rheumatoid Arthritis, SLE Auto Immune Haemolytic Anemias.
- (iii) Drugs e.g. Pencillin.

Out of these, immune mechanism is the most important in newborn and of these Iso Immune is more important than others.

Rh-incompatibility is most important because it is more severe. Rh-incompatibility is rare during first pregnancy and only occurs in 1% of the cases. In subsequent pregnancies its chance increases

Haemolytic disease due to minor blood group incompatibility is rare.

### DISCUSSION

- Q. 1. What are the blood groups of the other children of Fateh Bibi?
 

Ans. There are no records.
- Q. 2. What proportion of patients do not respond to anti D. injection given to the mother?
 

Ans. Ideally speaking 100% of the patients should respond but due to leakage of foetal blood during early pregnancy, tubal pregnancy and abortions 5 to 10% of the patients do not respond.
- Q. 3. What is the role of phenotype in Rh-incompatibility?
 

Ans. In our country about 15% of the population suffer from Rh-incompatibility, and about half of the off-springs are Rh-ve who escape Rh-incompatibility.
- Q. 4. As anti A and anti B are of IgM type, how do they cross placenta in ABO incompatibility?
 

Ans. ABO incompatibility usually occurs in mothers of blood group O because they produce immunoglobins of IgG variety which cross placenta and cause haemolytic disease of the newborn.
- Q. 5. The baby was exchanged with O-ve blood whereas her blood group was A negative, why?
 

Ans. Ideally she would have been exchanged with A-ve she was exchanged with O-ve blood.

PROF. M. SALEEM AKHTAR (*Gynae & Obs*)

1. Antenatal care in Pakistan is very poor and needs marked improvement. This patient although being a relative of Deputy Medical Superintendent of one of the largest hospitals for women in Pakistan was neither investigated nor treated properly.
2. Minor blood group antigens like Kell, Duffy, Lutheran, Lewis, Kidd etc. also need to be investigated properly and their antibody titers should be done. Blood transfusions in the child bearing life of a female should be avoided as far as possible as it leads to antibody development in them against the above mentioned antigens.

3. It is not necessary that anti-D is given within 48 hours of delivery to the Rh-negative mother. It can be given even the 5th or 7th day.
4. Such cases with bad obstetric history need a well trained team of paediatricians to be present at time of delivery.

DR. SAJID MAQBOOL (*Peds.*)

1. Of 100 Rh negative mothers with Rh positive fetus, 84 may not get immunized at all. 7-8 will demonstrate antibodies 6 months after delivery and 7-8 will demonstrate antibodies during the next pregnancy.
2. In haemolytic anemias. occasionally babies with positive coombs test but no Rh or ABO incompatibility are seen. These are cases of minor group incompatibility.

3. When coomb test is positive but no blood group incompatibility is found, then other auto immune haemolytic anaemias of mother as S.L.E., Rheumatoid arthritis, may be considered. Occasionally these are drug related.
4. Enzymatic Haemolytic disease of the newborn is coombs negative. Peripheral blood picture is very important in these cases.
5. As important side effect of exchange transfusion is infection. For this, antibiotics are started and when culture is negative they are stopped. They are closely observed for hypoglycemia during exchange transfusion. Blood used for exchange transfusion should be fresh otherwise side effects of hyperkalemia and thrombocytopenia occur. These babies develop anaemia due to normal expansion of blood volume and physiological anaemia may be relatively more prominent in these babies at the age of 3-6 weeks.