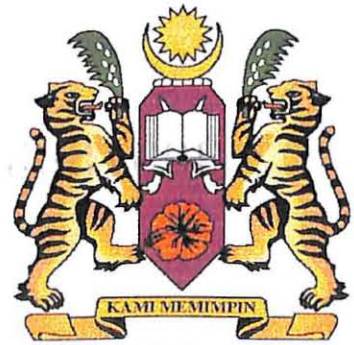
A STUDY OF ABO HAEMOLYTIC DISEASE OF THE NEWBORN IN HOSPITAL OF UNIVERSITI SAINS MALAYSIA KELANTAN

By:

DR SALMAN MOHD SAHID

Dissertation submitted in partial fulfillment of the requirements for the degree of Master of Medicine (Pathology).



Universiti Sains Malaysia

November 2001

ACKNOWLEDGEMENTS

I am in great debt to Dr Rapiaah Mustaffa, my supervisor and lecturer of Haematology Department HUSM for her generous help, advice and innumerable suggestion for improvements through out this project.

Many thanks to Ass Prof Dr Normah, Dr Narazah and Dr Rosline who has given many suggestion especially in the early part of the project. Special thank to Ass Prof Dr Mohd Shukri Othman, Head of Obstetric and Gynaecology HUSM for allowing his patients to be chosen for the study.

I am also acknowledge my gratitude to doctors and nurses of the Labour Room, HUSM for the help while collecting the specimens and laboratory technologists for the help while processing and analysing the specimens. Not to forget, my Community Medicine collegues who provide great help in analysing stastitical part of the data.

Most of all, I am grateful for the understanding and support of my wife and family during the hours devoted to this project.

TABLE OF CONTENTS

Contents *Page*

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBRREVIATIONS

ABO HDN	ABO haemolytic disease of the newborn
ADCC	Antibody-dependent cell-mediated cytotoxicity
DAT	Direct antiglobulin test
EDTA	Ethylenediamine tetra-acetic acid
ELAT	Enzyme-linked antiglobulin test
ELISA	Enzyme-linked immunosorbent assay
G6PD	Glucose-6-phospatase dehyrogenase
Hb	Haemoglobin
HUSM	Hospital of Universiti Sains Malaysia
NADPH	Reduced nicotine adenine dinucleotide phosphate
NICU	Neonatal intensive care unit
NNJ	Neonatal jaundice
NRBC per 100 WC	Nucleated red blood cell per hundred white cells
SD	Standard deviation

ABSTRACT (IN MALAY LANGUAGE)

Tujuan kajian ini adalah untuk menganalisa samada ujian-ujian rutin serologi dan hematologi makmal, boleh di gunakan untuk pengesanan awal penyakit hemolisis ABO bayi dan mendapatkan data-data untuk kajian epidemiologi berkenaan penyakit ini.

Kajian ini adalah secara 'cross-sectional' perbandingan ke atas bayi-bayi yang di lahirkan oleh ibu-ibu yang mempunyai kumpulan darah O resus positif di Bilik Bersalin, HUSM dari Oktober, 2000 hingga Jun, 2001. Spesimen darah dari talipusat bayi-bayi yang memenuhi kriteria diambil dan di uji untuk hemoglobin, bilirubin, pengiraan reticulosit, DAT, pengiraan sperosit dan pengiraan NRBC per 100 WC. Kemudian keputusan ujian-ujian tersebut dianalisa secara statistik. Data-data gambaran klinikal dan pengurusan rawatan bayi-bayi di ambil dari buku rawatan pesakit dan hubung-kaitnya dengan keputusan ujian darah dari tali-pusat bayi dikaji. Anggaran insiden dan keterukan penyakit hemolisis ABO bayi di buat dengan data-data yang di perolehi.

Keseluruhannya, 85 bayi iaitu 34 dengan ketidak-serasian ABO dan 51 dengan keserasian ABO memenuhi kriteria untuk kajian ini. Hemoglobin, pengiraan sperosit dan DAT di dapati mempunyai perbezaan yang sah secara statistik di antara kumpulan yang mempunyai ketidak-serasian ABO dan yang mempunyai keserasian ABO. Secara klinikal, lima bayi yang mempunyai ketidak-serasian ABO di dapati jandis dengan dua

daripada mereka telah menerima rawatan terapifoto dan tiada 'exchange transfusion' di perlukan. Insiden ketidak-serasian ABO di kalangan bayi-bayi di HUSM ialah 15.6%. Insiden penyakit hemolisis ABO bayi ialah 2.3%. Insiden bagi bayi yang mempunyai ketidak-serasian ABO memerlukan terapifoto di sebabkan penyakit hemolisis ABO bayi ialah 6.7% dan insiden untuk semua bayi memerlukan terapifoto di sebabkan penyakit ini pula ialah 0.92%.

Tiada hubung-kait yang jelas di antara gambaran klinikal dan keputusan ujian makmal. Ujian darah menerusi talipusat bayi, tidak boleh di cadangkan sebagai cara untuk ujian pengesanan awal untuk penyakit hemolisis ABO bayi. Ujian darah talipusat bayi adalah tidak sensitif dan spesifik berkemungkinan kerana keadaan penyakit tersebut yang tidak serius di HUSM. Insiden dan keterukan penyakit hemolisis ABO bayi di sini adalah hampir menyamai peratusannya di Amerika Utara dan Eropah.

ABSTRACT (IN ENGLISH)

The study was to evaluate whether the routine serological and haematological laboratory tests could be used for an early diagnosis of ABO HDN and to obtain epidermiological data.

This is a comparative cross-sectional study of newborn babies born to blood group O rhesus positive mothers in labour room of HUSM from October, 2000 to June, 2001. Specimens from cord blood of suitable babies were collected and investigated for haemoglobin, bilirubin, reticulocytes count, DAT, spherocytes count and NRBC per 100 WC. The results were analysed statistically. The clinical features and management data of ABO incompatible babies were taken from management file and correlation made with the cord's blood findings. The incidence and severity of ABO HDN were also estimated from the data.

Altogether 85 babies ie 34 ABO incompatible and 51 ABO compatible. The haemoglobin, spherocytes count and DAT showed a statistically significant difference between ABO incompatible and ABO compatible babies. Clinically five babies of ABO incompatible noted to be jaundice with two of them received phototherapy but exchange transfusion was not needed in any of them. The incidence of ABO incompatible infants in HUSM is 15.6%. The incidence of ABO HDN is 2.3%. The incidence of ABO

incompatible infants requiring phototherapy due to ABO HDN is 6.7% and the incidence of all infants requiring phototherapy due to ABO HDN is 0.92%.

There is poor correlation between the clinical features and laboratory findings. The cord blood tests therefore can not be recommended as method of early diagnosis of ABO HDN. The cord blood tests were not sensitive and specific probably due to mildness of ABO HDN in HUSM. The incidence and severity of ABO HDN here are almost comparable to the figures of North America and Europe.

Chapter 1

INTRODUCTION

1.0 INTRODUCTION

1.1 DEFINITION

Haemolytic disease of the newborn (HDN) is a condition in which the life span of the infant's red cells is shortened by the action of specific antibodies derived from the mother by placental transfer. The disease begins in intra-uterine life and is therefore correctly described as haemolytic disease of the fetus and newborn but the simple term haemolytic disease of the newborn has been used for a long time and can be taken to include haemolytic disease of the fetus (Mollison et al.1997).

HDN is also defined as a disease characterised by the destruction of fetal / newborn red cells resulting from the placental transfer of maternal alloantibody (Strohm 1995).

The placental transfer of maternal alloantibody is only of IgG class. The commonest IgG red cell antibodies in human serum are anti-A and anti-B and relatively high concentrations are found only in group O subjects (Mollison et al. 1997). This is because the group O individuals are "naturally" pre-sensitised to A and B antigens by exposure to ABO-like substances found in food or other exogenous sources (Foerster 1992). The anti-A and anti-B occurring in group B

and A subjects respectively, are almost of IgM variety that cannot cross the placental barrier.

The disease cause by these anti-A and anti-B are usually termed as ABO HDN and for practical purposes, it is restricted to A or B individuals with mothers of O (Mollison et al.1997). However, group B infants of group A (particularly A_2) mothers occasionally are affected (Strohm 1995).

There are many other antibodies that can cause HDN. The list of antibodies in table 1.1 below, includes most but not all of those which can occur as IgG and known to have caused HDN.

Table 1.1: Alloantibodies reported to cause HDN (Adapted from Mollison et al. 1997).

Within the Rh system	Anti-D, -c, -C, -C^w, -C^x, -e, -E, -Ew, -ce, -Ce^s, -Rh32, -Go^a, -Be^a, -Evans, -LW
Outside the Rh system	Anti-K, -k, -Ku, -Kp^a, -Kp^b, -Js^a, -Js^b, -Fy^a, -Fy3, -Jk^a, -Jk^b, -M, -N, -S, -s, -U, -Vw, -Far, -M^v, -Mit, -Mt^a, -Mur, -Hil, - Hut, -En^a, -PP, -P^k, -Lu^a, -Lu^b, -Lu9, -Di^a, Di^b, -Yt^a, -Yt^b, -Do^a, -Co^a, -Wr^a
Antibodies to high-incidence antigens	Anti-At^a, -Jr^a, -Lan, -Ge
Antibodies to low-incidence antigens	Anti-Bi, -By, -Fr^a, -Good, -Rd, -Re^a, -Zd

1.2 HISTORICAL ASPECTS

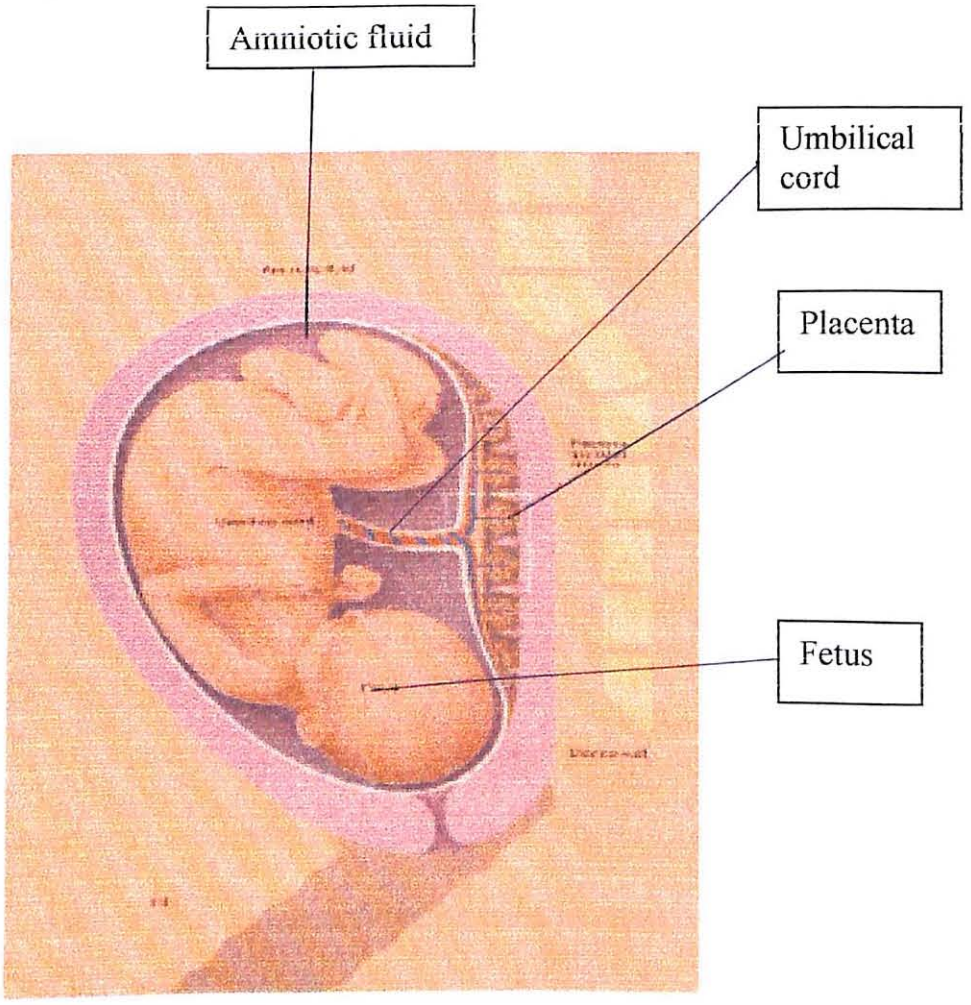
In 1609, a French midwife, Louyse Bourgeois, writing in the popular Paris press, was the first to describe haemolytic disease of the newborn. She reported the birth of twins: the first twin was bloated with fluid (hydropic) and died shortly after birth; the second appeared well but rapidly became jaundiced (icterus gravis), lay in a position of opisthotonos and died (kernicterus). These two conditions ie hydrops fetalis and kernicterus (yellow staining of the brain) were described in detail by pathologists at the turn of the century but were not thought to be the same entity until 1932 (Bowman 1998).

In 1932, Diamond and co-workers showed that hydrops fetalis, icterus gravis, and kernicterus were simply different spectra of the same disease characterised by hemolytic anaemia, extramedullary erythropoiesis, hepatosplenomegaly and the out-pouring of immature nucleated red blood cells (Naiman 2001). The ABO HDN was however, first described in 1944 by Halbrecht (Brouwers et al. 1988a).

1.3 PATHOPHYSIOLOGY

In humans, the transfer of antibodies from mother to fetus takes place only via the placenta. The only immunoglobulin transferred is IgG, which is bound by an Fc receptor on the plasma membrane of the placenta. The transfer of IgG is an active process and takes place only from mother to fetus and not in the reverse direction.

Figure 1.3: Diagram showing the fetus in relation to placenta and uterine wall.



(Adapted from Ortho Diagnostics, 1968).

The sensitisation of mother's immune system or alloimmunisation increase with each incompatible pregnancy. The primary stimulus for immunisation, in addition to exposure to ABO-like substances such as found in food, can also be a previous blood transfusion or abortion. Formation of Rh antibodies is the most common form of alloimmunisation to give rise to clinically important disease. However during pregnancy, ABO immunisation occurs more often than Rh immunisation (Wells and Isbister, 1997).

ABO HDN is quite different from HDN due either to anti-D or other blood group antibodies. Anti-A and anti-B, which bind complement in adults, cause violent, life-threathening intravascular hemolysis after transfusion of ABO-incompatible blood. However fetal ABO HDN is usually much milder than D, c and K forms of HDN.

Several reasons can be listed for the paradoxical mildness of ABO HDN. First, there are fewer A and B antigenic sites on the fetal RBC membrane. Also, anti-A and anti-B (with very rare exception; Pujol et al. 1991) do not activate complement on the fetal RBC membrane (Wang and Desforges, 1971; Brouwers et al. 1988b). Second, anti-A and anti-B are mostly IgM, which does not cross the placenta (Ramasethu and Luban, 2001). Third, the small amounts of IgG anti-A and anti-B that do traverse the placenta have myriad antigenic sites other than those on RBCs, other tissues, and secretions to which they may bind. Only a very small proportion of the minor amount of anti-A or anti-B that crosses the placenta

adheres to antigen on the fetal RBC membrane (Bowman 1998). Fourth, the severity may be related to IgG subclass. IgG2 constitutes a significant component of anti-A and anti-B antibody; this subclass of IgG is transported less readily across the placenta than are IgG1 or IgG3 and is a less efficient mediator of macrophage-induced red cell clearance (Ramasethu and Luban, 2001).

Table 1.3: Properties of human IgG subclasses (Parslow 1997).

	IgG1	IgG2	IgG3	IgG4
Abundance (% of total IgG)	70	20	6	4
Half-life in serum (days)	23	23	7	23
Placental passage	+++	+	+++	+++
Complement fixation	+	+	+++	–
Binding to Fc receptors	+++	+	+++	–

The relative concentrations of the four subclasses vary somewhat among individuals. It appears that the propensity to produce IgG antibodies of one subclass or another is at least partly an inherited trait (Parslow 1997). The antibodies with the subclass with the highest titre, strongly influence the result of the DAT, and in many cases of ABO incompatibilities these are IgG2 antibodies. However, it has been reported that in infants with severe ABO HDN, the IgG subclasses bound to cord red cells are IgG1 and / or IgG3 in addition to IgG2 (Ukita etal. 1989).

1.4 INCIDENCE

Incidence of ABO HDN depends on incidence of ABO incompatibility. It should be noted however that ABO incompatibility is not synonymous with ABO HDN. In other words, ABO HDN is the extreme end of the spectrum of ABO incompatibility.

ABO hemolytic disease must be defined before its incidence can be estimated. For example, taking the criterion of the development of jaundice within 24 hours of birth, the incidence was estimated by Halbrecht (1951) to be one in 180; taking the faintest trace of jaundice in the first 24 hours as the criterion the incidence was found by Valentine (1958) to be as high as one in 70. In a study by Meberg and Johansen (1998), the ABO incompatible babies that required phototherapy were one in 106 or 0.94% of all term infants.

Cases of HDN due to anti-A or anti-B which are severe enough to need exchange transfusion are relatively rare for examples three of 8000 births (Ames and Lloyd 1964); six of 5704 newborn infants (Voak and Bowley 1969); none amongst 534 infants born to group O mothers (Meberg and Johansen 1998).

A higher incidence has been found in some other populations. The incidence of ABO HDN was found to be substantially higher in Venezuela, in which about 30% of ABO incompatible infants have signs of haemolytic disease

compared with 20% or less in European and North American populations (Cariani et al. 1995). The disease was found to be commoner in Blacks by Kirkman (1977). Peevy and Wiseman (1978) also support the evidence concerning racial differences but not in the severity of ABO HDN between black and white infants. In a survey in Nigeria, the frequency of ABO HDN is about 5% of births (Worlledge et al. 1974).

Al-Jawad et al. (1985) in their study concluded that ABO HDN was about as common in Arabs as in Blacks and that the disease tended to be more severe in Arab than in Europeans; exchange transfusion for ABO HDN was carried out on one in every 500 newborn Arab infants. Romano et al. (1994) in their study noted about one in 300 of all newborn infants in Venezuela need exchange transfusion.

However, a study in multi-ethnic hospital in USA concluded that there was no significant difference in prevalance of clinical disease, which requires exchange transfusion among Asian, Black, Hispanic and Caucasian infants (Toy et al. 1988). Their study shows that in a sample of over 10,000 infants, ethnic differences were detectable in the laboratory but not in clinical disease.

Locally, in HUSM, a study by Siti Aesah (1995), from the period of October, 1994 – January, 1995, found that, out of total of 58 babies with neonatal jaundice (NNJ) who were admitted to Neonatal Intensive Care Unit (NICU), only

two need exchange transfusion and there were due to ABO HDN. The study also concluded that 12.1% of the NNJ babies were ABO HDN.

Ho (1992) has review many studies on incidence of ABO incompatibility among jaundice baby. The review is summarised in table 1.4.

Table 1.4: The incidence of ABO maternal – infant incompatibility among jaundice baby.

Country	Year	% among cases of jaundice
Australia	1983	7.1
China, Beijing	1989	20
Hong Kong	1970	15.6
Hong Kong	1986	12.5
Singapore	1988	16.6
Singapore	1991	15.9
India, New Delhi	1987	12.2
India, Madras	1987	38.2

In relation to DAT positive, the incidence in the cord blood of ABO incompatible babies are about 25% -30% (Bowman 1989). Toy et al. (1988) have done a prevalence study of ABO maternal-infant incompatibility in Asians, Blacks, Hispanics and Caucasians from 10 611 consecutive infants born over a six

years period. They have found that the prevalence of a positive DAT among group A infants born to O mothers was different among the four groups and highest in Asians (50%), followed by Hispanics (42%), Blacks (40%) and Caucasians (31%). The positive DAT rates were not different among the four groups of B infants born to O mothers with Asians showing positivity of 39%. The prevalence of positive DATs in all births was 6, 5, 5 and 4% respectively in the four groups.

Another study in Bangkok, Thailand (Chuansumritet al. 1997) found that the positive rate of DAT in the ABO incompatible group were 54.5% by a conventional spin-tube technique and 50% by a gel technique. In the ABO compatible the positive rate of the DAT were 2.6% by the conventional and 10.5% by the gel technique.

1.5 CLINICAL FEATURES

1.5.1 SPECTRUM OF HDN

HDN irrespective of whether it cause by ABO, Rhesus or other alloantibodies can occur in various forms.

In its least severe form, HDN manifests itself as a mild haemolytic anaemia. The infant's red cells, coated with maternal IgG antibodies, are removed prematurely from the circulation, causing slight jaundice (maximum on the second to third days of life) and mild anaemia during the second week of life. More severely affected infants show severe hyperbilirubinaemia in the neonatal period, a condition which was called icterus gravis neonatorum. Prompt treatment with exchange transfusion is necessary to prevent bilirubin impregnation of the basal ganglia and neurological damage, a condition known as kernicterus. This condition may be fatal, or lead to serious neurological deficit, with deafness, mental retardation, choreo-athetosis and spasticity.

In the most severely affected cases, profound anaemia develops in utero, and intrauterine death may occur at any time from the eighteenth week of gestation. Affected fetuses are pale and oedematous, with marked ascites. The placenta is bulky, swollen and friable. This condition is known as hydrops fetalis, and had a high mortality rate until ultrasound-guided intravascular transfusions

and improved intensive care facilities for very premature babies were introduced. The pathophysiology of hydrops is not fully understood, but extravascular haemolysis with fetal anaemia seems to play a major role by stimulating extramedullary erythropoiesis in the liver, with distortion of the hepatic circulation, leading to portal hypertension and impaired albumin production. Hypoalbuminaemia leads to ascites, oedema and pleural / pericardial effusions. In addition, the severe anaemia leads to cardiac failure and tissue hypoxia, which damages the endothelium, leading to fluid extravasation into extravascular space.

1.5.2 COMMON MANIFESTATION

ABO HDN is far more comman than Rh HDN but clinical presentation is usually mild and rarely responsible for fetal deaths (Ramasethu and Luban, 2001). The most common manifestation is jaundice which appear during first 24 hours of life, but it is not as pronounced and rarely is sufficiently severe to cause complications such as kernicterus. The anaemia is correspondingly mild, pallor is uncommon and hydrops fetalis is exceedingly rare. Mild degrees of hepatosplenomegaly may be observed (Foerster 1992).

First-born infants are affected as frequently as those born subsequently in which they are 40% - 50% of all HDN (Ramasethu and Luban, 2001). In families in which ABO HDN is mild, an affected infant may be followed by a clinically unaffected infant. On the other hand, when severe disease occurs it is likely to be followed by similarly severe disease in subsequent infants of the same blood group (Mollison et al. 1997).

1.6 LABORATORY FINDINGS

1.6.1 SEROLOGY

ABO GROUP: Mothers of infants with ABO HDN almost invariably belong to group O. However, in one series of 45 cases, reported by Munk-Andersen (1958), the mother was group O in 43 instances and subgroup A2 in the remaining two; A2 mothers produced much stronger 'incomplete' anti-B than A1 mothers. The affected infants are either belong to group A or B.

THE DIRECT ANTIGLOBULIN TEST (DAT): The infant's red cells often give a negative or only weakly positive reaction to the DAT (Ukita et al. 1989). This failure of antibody-sensitised fetal cells to agglutinate with antiglobulin sera may be a function of the smaller number of antibody molecules sensitising these fetal cells (Ramono et al. 1973), which in turn may, at least in part, reflect the greater distance between sites in fetal cells as compared to the distance in adult cells (Voak and Williams, 1971).

Merry et al. (1984) has found correlation between agglutination strength and the number of IgG molecules bound per cell in the DAT. In normal subjects with a negative DAT the number of IgG molecules per red

cell was found to be in the range 5 – 90. The findings of Jeje et al. (1984) were almost identical to this. Some studies has found that when the spin-tube antiglobulin test is used, the minimum number of antibody molecules which can be detected is about 100 – 150 (Romano et al. 1973; Burkart et al. 1974; Stratton et al. 1983).

In a study by Chuansumrit et al. (1997) which compared DAT using gel technique and the conventional spin-tube technique, found that the positive rate in the ABO incompatible group was similar by both techniques. However the scores by the gel technique were higher than those of the conventional technique.

IgG ANTI-A AND ANTI-B OF MOTHERS: The test can be done by treating the mother's serum with a reducing agent to inactivate IgM antibodies and then determine the anti-A or anti-B titre by IAT using an anti-IgG serum (American Association of Blood Banks, 1996). Using this method a titre of 512 or more was found to be very suggestive of haemolytic disease (Mollison et al.1997).

1.6.2 HAEMATOLOGICAL

HAEMOGLOBIN CONCENTRATION: Normal cord blood value is 15.3±1.3 g/dl (Diagne et al.1995). Anaemia is taken as Hb concentration < 14.0 g/dl. In moderately severe ABO HDN the Hb concentration of cord blood may be below normal limit. ABO HDN is a shot-lived affair and it is unusual for anaemia to be found after the first 2 weeks or so of life.

RETICULOCYTOSIS: A slight increase in reticulocytes is common feature in HDN due to ABO incompatibility (Rosenfield 1955). In the series of fairly severe cases collected by Crawford et al. (1953), the reticulocytes count exceeded 15% in six of 11 cases.

ERYTROBLASTAEMIA: The same study by Crawford et al (1953) also noted 5 of the 11 cases were having 30 or more nucleated red cells per 100 leukocytes. Latest study by Hanlon-Lundberg and Kirby (2000) found an association between ABO incompatibility and elevation in NRBC even with mild clinical courses.

SPHEROCYTOSIS: Spherocytes are cells which are more spheroidal (less disc-like) than normal red cells. Their diameter is less and their thickness greater than normal. Only in extreme instances are they almost spherical in

shape. Spherocytes has been described as a feature of ABO HDN but not seen in Rh HDN (Oski and Naiman, 1982).

SERUM BILIRUBIN: Fetal serum bilirubin is maintained at a low level (<2.0 mg/dl) exclusively by placental clearance. Even in situations of markedly increased fetal bilirubin production fetal serum bilirubin concentration rarely exceed 5 to 7 mg/dl (Whitington and Alonso, 1998).

1.6.3 SPECIAL TESTS

IgG SUBCLASSES OF ANTI-A AND ANTI-B: Anti-A and anti-B from pregnant women are at least partly IgG2. Macrophages carrying the high-affinity FcIIa receptor mediate lysis of red cells sensitised with IgG2 anti-A, although not that of cells sensitised with IgG2 anti-Rh D (Kumpel et al. 1996). Presumably, therefore, IgG2 anti-A and anti-B play a part in red cell destruction in those infants with ABO HDN whose macrophages carry the high-affinity FcIIa receptor.

ANTIBODY-DEPENDENT CELL-MEDIATED CYTOTOXICITY ASSAYS (ADCC) AND ANTIGEN DENSITY OF A AND B: Brouwers et al (1988a) in a study of ABO HDN has measured the lytic effect of IgG anti-A or anti-B from maternal blood samples by ADCC with monocytes as effector cells. The antibodies were considered to induce lysis when more than 10% of the target cells were lysed. In the cord blood samples they have also measure the relative antigen density of the A or B antigen by ELISA technique. The relative antigen density was expressed as the percentage of the reaction with the most strongly reacting cord-blood red cells and was considered to be high when the antigen density was more than 65%. They have found that the degree of lysis was strongly affected by the number of A or B sites on the red cells.

DIRECT ENZYME-LINKED ANTIGLOBULIN TESTS (ELAT): Kiruba et al (1988) has studied usefulness of ELAT in detecting sensitised cells in haemolysis of the newborn due to ABO incompatibility. The technique which used an ELISA reader to measure absorbance of the sample was found to be more sensitive than the DAT.

1.7 MANAGEMENT

1.7.1 ANTENATAL SCREENING

Many workers have tried to use immunoglobulin class and titer of maternal ABO antibodies to predict ABO HDN. These tests are laborious and at best demonstrate the presence of IgG maternal antibody but do not correlate well with the degree of fetal RBC destruction (Kennedy and Abdul Waheed, 1999). Consequently, detection of ABO HDN is best done after birth.

1.7.2 EXCHANGE TRANSFUSION

The key to the management of HDN is exchange transfusion, which was introduced by Wallerstein in 1945 (Bowman, 1998). Since severe anaemia is very uncomman, the main indication for exchange transfusion is the threat of serious hyperbilirubinaemia, leading to kernicterus. When exchange transfusion is judged to be necessary, group O blood should be used. Provided that the donor's plasma has been screened so as to exclude donors with potent anti-A or anti-B, the antibodies in the transfused plasma are unlikely to exacerbate the haemolytic process.

1.7.3 PHOTOTHERAPY

The mode of action of phototherapy in lowering serum bilirubin concentration is that, on exposure to light, particularly in the region of 420 – 480 nm, bilirubin is converted to the non-toxic pigment, biliverdin. In those full-term infants with ABO HDN whose serum bilirubin concentrations threaten to rise to dangerous levels, phototherapy is often sufficient to control situation.

1.8 RATIONALE OF THE STUDY

Since 1944 when the ABO HDN was first described by Halbrecht, many investigators have tried to find a simple test to predict whether the baby will be affected.

Toy et al. (1988) considered DAT to be the best laboratory predictor of severity of ABO HDN. Menon and Mohapatra (1987) found the quantitative estimate of spherocytes a good predictor of ABO incompatibility, whereas the DAT was a better predictor of severe haemolytic disease. However, Quinn et al (1988) mentioned that, in the individual case, Coombs' positivity and / or a strong positive elution test may be a helpful predictor of jaundice, but not of its severity.

Kiruba et al (1988) introduced ELAT as more sensitive test than DAT. However, ELAT may be good for epidemiology study but not good enough for routine use since it specificity still low. Later Chuansumrit et al (1997) have compared the DAT done using the conventional spin-tube technique with a simple and technically less demanding gel technique. They found that although the positive rate of DAT in the ABO incompatible group was similar, the scores by the gel technique were higher than those of the conventional technique.

Brouwers et al (1988a) suggested that the combination of the antibody-dependent cell-mediated cytotoxicity (ADCC) assay with the density of A or B

antigens on cells provides a good screening test for ABO incompatibility. The drawback of the tests was that it not widely available and expensive for routine use. Further more in the West, some clinicians (e.g. Quinn et al 1988) were doubted whether ABO incompatibility matters. A population based study of 2463 infants with 554 ABO incompatibility by Meberg and Johansen (1998) has found that no exchange transfusion required in any of the infants. In fact, no kernicterus has occurred in their population since 1970.

There were however significant different of behaviour of ABO maternal-infant incompatibility among races. The study in the multiethnic hospital in USA by Toy et al (1988) found that the prevalence of positive DAT results were highest in Asian followed by Black, Hispanic and Caucasian. There were also different in incidence and severity among Nigerian's Black and Arab. The Arab for example was reported to required exchange transfusion for ABO HDN in one out of 500 newborn infants.

There were not many studies in Malaysia in the subject of ABO HDN per se. Many studies were on neonatal hyperbilirubinaemia or jaundice. The local HUSM study, on neonatal indirect hyperbilirubinaemia by Siti Aesah (1995) in Neonatal Intensive Care Unit (NICU) from period of October, 1994 – January, 1995 has studied total of 58 babies.