

The role of maternal anti-A and anti-B antibody titers in predicting ABO hemolytic disease of the newborn

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Abstrak

Telah dilakukan penelitian terhadap 268 persalinan ibu golongan darah O dengan bayinya golongan darah A atau B. Kemampuan ibu golongan darah O memproduksi antibodi anti-A dan anti-B tidak beda bermakna ($p < 0,05$). Ditemukan 94 bayi (35,1%) mengalami ikterus potensial dan 174 bayi (64,9%) ikterus tidak potensial. Untuk memprediksi kelahiran bayi ikterus potensial diperoleh titer antibodi anti-A dan anti-B ibu $\geq 1/256$ sebagai cut-off point dengan sensitifitas 83,33% dan spesifisitas 78,21%, nilai prediksi positif 79,27% dan nilai prediksi negatif 17,57%. Pada titer antibodi anti-A dan anti-B ibu $\geq 1/256$, risiko dilahirkannya bayi ikterus potensial secara bermakna menjadi 18 kali lebih besar dibandingkan titer $< 1/256$ (RO 18,64 ; IK 95% = 6.18 - 56.18).

Abstract

A study has been conducted on 268 blood group O delivering mothers and their related blood group A and B newborn infants. It revealed that the capability of mothers to produce anti-A and anti-B antibodies did not differ significantly from each other ($p > 0.05$). Ninety four (35.1%) of the newborns developed potential jaundice while the others did not. To predict the birth of a baby with potential jaundice, a maternal anti-A or anti-B antibody titer of $\geq 1/256$ was considered to be the cut-off point with a sensitivity and specificity of 83.33% and 78.21% respectively and a positive predictive value of 79.27% and a negative predictive value of 17.57%. If the maternal anti-A or anti-B antibody titer was $\geq 1/256$ the risk for giving birth of a baby with potential jaundice rose significantly 18 times compared to those with titers of $< 1/256$ (OR 18,64 ; CI 95% = 6.18-56.18).

Keywords: ABO incompatibility, anti-A/B antibody titers, hemolytic disease of the newborn

ABO hemolytic disease of the newborn (ABO-HDN) is at present the most frequently hemolytic disease found in newborns after anti-Rh0 (anti-D) preventive measures against Rhesus hemolytic disease have been found out.^{1,2} ABO-HDN is more frequently found in blood group A or B newborn infants born from blood group O mothers and the occurrence significantly differs from ABO incompatibility cases in blood group A or B mothers.^{1,2} This group represents the pregnancy at risk for ABO blood group incompatibility for the occurrence of neonatal jaundice. This is actually caused by the fact that anti-A and anti-B antibodies of blood group O mothers is in general of IgG class origin which can pass transplacentally while in the case of blood group A or B mothers it is of IgM origin which can not pass across the placenta.^{3,4} Blood group O mothers have naturally already anti-A and anti-B antibodies in their blood. The fetal red cells immunization across

the placenta in OA or OB incompatible pregnancies may cause an immune response in the mother which may increase those levels of anti-A and anti-B antibody titers. Besides fetal red blood cell immunization, the level of the maternal anti-A and anti-B antibody titers depend also on the environment. The incidence of ABO-HDN in slum areas is found to be higher than in favorable healthy living areas.⁵ This is thought to be as a consequence of the fact that in slum areas many E.coli bacteria and Ascaris lumbricoides worms are still prevailing while in those organism a substance resembling A or B red blood cell component is found.^{6,7} Continuous and recurrent exposure may cause a secondary immune response thus resulting in the presence of anti-A and anti-B antibodies in the mother. In pregnant mothers with high titers of anti-A or anti-B antibodies, the risk for the newborn to contract ABO-HDN becomes thus also higher.^{8,9}

The aim of this study is to find out the cut-off point of the maternal anti-A and anti-B antibody titers which may function as a predictor in the occurrence of potential jaundice in ABO-HDN.

MATERIALS AND METHODS

The subjects of this study consisted of blood group O delivering mothers with their A or B blood group newborn infants. During pregnancy and labor the mothers had not received blood transfusion so far while the newborn infants were all live births which a birthweight of > 1500 gram or gestation period of > 32 weeks, all without mayor congenital malformations. Samples were patients from Dr.Cipto Mangun- kusumo General Hospital, the Budi Kemuliaan Maternity hospital and also from four community health centers scattered all over Jakarta on April 1995 to January 1997. Maternal peripheral blood samples right before delivery were obtained and cord blood samples of the newborn infants after birth. Seroim-

analysis were performed. To find out the anti-A and anti-B antibody titers as predictor of the occurrence of potential jaundice, a calculation was made on the sensitivity and specificity at the cut-off points of 1/64, 1/128, 1/256, 1/512 and 1/1024 titers and plotted on the receiver operating characteristic (ROC) curve.

RESULTS

Two hundred sixty eight blood samples of the mother and of its respective newborn infants had been collected, consisting of blood group O mothers and cord blood group A or B of the newborn. The distribution of anti-A and anti-B antibody titers in the serum of the mother by the newborn's blood group is shown in Table 1.

Table 1. Maternal anti-A and anti-B antibody titers by the newborn's blood group

Maternal anti-A and anti-B antibody titers	Number of newborn		Number of sample (n=268)	Percentage (100.0%)
	Blood group A	Blood group B		
1/1 - 1/32	21	26	47	17.6
1/64 - 1/128	54	57	111	41.5
1/256 - 1/512	34	44	78	29.2
1/1024 - 1/2048	14	15	29	10.9
> 1/2048	1	2	3	0.8
Total	124	144	268	100

$$\chi^2 = 0.32 ; df = 4 ; p = 0.985 ; NS$$

munologic antiglobulin tests (Coombs' test) were performed in the mothers and newborns blood as soon as possible. The maternal anti-A and anti-B antibody titers were determined and the cord blood was divided into two groups, namely the potential jaundice (positive Coombs' test) and the non potential jaundice (negative Coombs' test). Design of the study were performed into two steps, the first step was a cross-sectional study to obtain the basic data, while the second step was a case-control study (nested case-control study) between the potential jaundice and the non potential jaundice groups. To distinguish between the two groups as a case group and control group, a matching was done of three variables influencing the occurrence of neonatal jaundice namely the gestation period, newborn blood group and the sex of the newborn. Data analysis was done with Chi-square test. Fisher's exact test with significance limit of $p < 0.05$ and by calculating relative risk (Odds ratio) with 95% confidence interval. Model of bivariat and multivariat

There was no significant difference found between the number of newborn with A and B blood group in any maternal titer group ($p > 0.05$), meaning that the capability of blood group O mothers in producing anti-A or anti-B antibodies was the same.

Results of antiglobulin test of the newborn's cord blood were divided into the potential jaundice group (positive Coombs' test) and the non potential jaundice group (negative Coombs' test). Newborn with potential jaundice have the potential to develop neonatal jaundice. Table 2 shows the distribution of newborn blood group by the results of the antiglobulin tests.

As many as 94 out of the 268 studied samples (35.1%) showed potential jaundice, those newborn had a tendency to develop neonatal jaundice. The probability of becoming potential jaundice in the blood group A or B newborn did not differ significantly ($p > 0.05$).

Table 2. Distribution of antiglobulin test by newborn's blood group

Antiglobulin test	Number of newborn		Number of sample (n=268)	Percentage (100.0%)
	Blood group A	Blood group B		
Positive (potential jaundice)	46	48	94	35.1
Negative (non potential jaundice)	78	96	174	64.9
Total	124	144	268	100

$\chi^2 = 0.27$; $df = 1$; $p = 0.606$; NS

Table 3 reveals result of sensitifity and specificity tests on the various cut-off points of maternal blood group O anti-A and anti-B antibody titers which was then also plotted as a curve on the receiving operation characteristic (ROC) chart.

percentage with a positive predictive value of 79.27% and negative predictive value of 17.57%. With those sensitivity and specificity values the cut-off point of maternal anti-A and anti-B antibodies to be 1/256. Plotting those sensitivity and specificity values on the

Table 3. Sensitivity and spesificity at various cut-off points of maternal anti-A and anti-B antibody titers

Maternal antibody titer	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
1/64	100	23.08	56.52	0
1/128	98.72	57.69	70	2.17
1/256	83.33	78.21	79.27	17.57
1/512	64.1	94.87	92.59	27.45
1/1024	30.77	97.44	92.31	41.54

At the maternal anti-A and anti-B antibody titer of 1/256 it was found a sensitivty of 83.33% and a specificity of 78.21% which comprised the highest

receiver operating charcteristic (ROC) chart a curve as follows will be seen (figure 1).

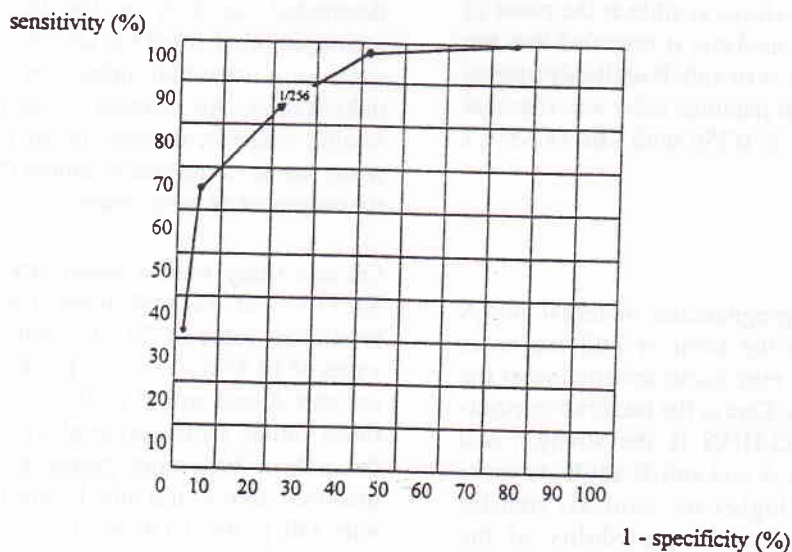


Figure 1. Receiver operating characteristic (ROC) curve

One of the factor influencing the severity of ABO-HDN is the strength and quantity of the mother's antibody cross transplacentally.¹⁰ After matching the potential jaundice and the nonpotential jaundice groups in the nested case-control method (gestation period, blood group and sex), a total of 78 samples each respectively was taken for case group and control group.

Table 4 shows the bivariat analysis, the influence of maternal anti-A and anti-B antibody on the antiglobulin test at the cut-off point of 1/256.

the quantity and quality of the antibodies, several other factors may also contribute to the severity of ABO-HDN among others the antibody subclass, variation of antigen subtype of the fetal red blood cells, the secretor system of the fetal tissue and body fluid, the antibody quantity and speed transfer transplacentally, the efficiency of the fetal mononuclear cells and the maturity of the fetus.^{1,2,10,11,12} After 32 weeks of pregnancy the transplacental transfer of IgG antibody increases speedly and at the end of mature pregnancy the amount of IgG molecules in the placental

Table 4. Influence of maternal anti-A and anti-B antibody titer on potential jaundice

Maternal anti-A and Anti-B titer	Antiglobulin test		Number of sample (n=268)
	Positive (potential jaundice)	Negative (non-potential jaundice)	
≥ 1/256	65	17	82
< 1/256	13	61	74
Total	78	78	156

$$\chi^2 = 56.79 ; df = 1 ; p = 0.000 ; OR 17.94 CI 95\% = 7.52 - 43.77$$

By the bivariat analysis it revealed that at the cut-off point of 1/256 of the maternal anti-A and anti-B antibody titer the probability of the birth of a newborn with potential jaundice was significantly greater than titers of < 1/256.

The multivariat analysis model was also performed on several other variables which on the bivariat analysis had a significant role on the occurrence of potential jaundice namely placental inflammation, the way the baby was born and the facilities available at the place of birth. On the multivariat analysis it revealed that the influence of maternal anti-A or anti-B antibody titer on the occurrence of potential jaundice baby was found at the cut-off point titer of ≥ 1/256 with OR 18.65; CI 95% = 6.18 - 56.18.

DISCUSSION

In ABO incompatibility pregnancies, maternal anti-A and anti-B antibodies in the form of IgG can cross transplacentally and thus may cause destruction of the newborn's red blood cells. One of the factors contributing the severity of ABO-HDN is the strength and quantity of maternal anti-A and anti-B antibody cross transplacentally.¹⁰ The higher the antibody transfer transplacentally the higher the probability of the destruction of the newborn's red blood cells. Besides

trophoblast increases so that at birth the newborn infant's number of IgG molecules is higher than the mother's.^{13,14}

To predict the occurrence of potential jaundice in ABO incompatible pregnancies it is important to know the cut-off point of the maternal anti-A and anti-B antibody titers so much so that monitoring action of the born baby can be intensified. The already sensitized red blood cells of the newborn can more easily be destructed not only on the fact of its condition of incompatibility itself but also because of other causes such as nosocomial infections, acidosis as well as dehydration. An increase of the bilirubin content following excessive destruction of red blood cells is already known to be able to hinder the baby's growth and development in later years.^{15,16,17}

On this study with a sensitivity and a specificity of 83.33% and 78.21% respectively with a positive predictive value of 79,27% and a negative predictive value of 17.57%, a cut-off point of 1/256 of the maternal anti-A and anti-B antibody titer was found. With those values, by the bivariat analysis it was found that the risk of becoming potential jaundice was at the maternal anti-A and anti-B antibody titer of ≥ 1/256 with OR 17.94; CI 95% = 6.18 - 56.18. On the bivariat analysis there were still other possible variables work-

ing synergically as well as antagonistically on the newborn's potential jaundice. After having performed a multivariate analysis on other variables contributing in the occurrence of the newborn's potential jaundice at that certain titer the ratio odds was OR 18.64; CI 95% = 6.18 - 56.18. The obtained data revealed that the titer of $\geq 1/256$ of the maternal anti-A and anti-B antibody the risk of the newborn infant with potential jaundice significantly became 18 times higher compared to those with low antibody titers ($< 1/256$).

This study was conducted on the middle to low socioeconomic class comprising the mayor of our whole population. For clinical application it can be suggested that in a blood group O delivering mother with a non O newborn infant, maternal anti-A and anti-B antibody titer $\geq 1/256$ on the antiglobulin test is a marker and warrant the health worker involved to intensify monitoring of the newborn infant. This is due to the fact that the risk for potential jaundice of the newborn becomes 18 times higher.

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