국내 임신부의 비예기항체 빈도와 신생아의 예후 분석

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Prevalence of Unexpected Antibodies in Pregnant Korean Women and Neonatal Outcomes

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Background: In pregnant women, the frequency of irregular antibodies that cause hemolytic disease of the fetus and newborn (HDFN) vary between study populations. The clinical manifestations of HDFN differ according to the specificities and degree of irregular antibodies. This study examined the frequency and nature of maternal alloimmunization and neonatal outcomes.

Methods: Pregnant women, who underwent irregular antibody screening for prenatal testing at an obstetrics clinic in a single center, were enrolled. Those who screened positive for irregular antibodies were selected as the test group, and age- and obstetrics history-matched pregnant women were selected as the control group to evaluate the pregnancy outcomes according to irregular antibodies.

Results: The prevalence of irregular antibodies was 2.78% (42/1,508). With the exception of an unidentified antibody, anti-D was the most frequently identified antibody, followed in order by anti-E and anti-Le^a. The rate of fetal death was higher in the test group (6/37, 16.2%) than in the control group (1/37, 2.7%) ($P=0.047$). Eight pregnant women had anti-C or anti-D, one woman had a stillbirth, and four living neonates developed hyperbilirubinemia. Of six pregnant women with anti-E alone or with other alloantibodies, three experienced a spontaneous abortion or stillbirth. Among the six newborns with maternal anti-Le^a and anti-Jk^a, four developed hyperbilirubinemia, but their mothers did not experience a spontaneous abortion or stillbirth.

Conclusion: The prevalence of unexpected antibodies among pregnant Korean women was 2.78%. A significant difference in neonatal outcomes was observed, including the death rate, prematurity, and hyperbilirubinemia, depending on the specificity of the unexpected antibody. (Korean J Blood Transfus 2019;30:23-32)

Key words: Hemolytic disease of the fetus and newborn, Alloimmunization, Hyperbilirubinemia, Pregnancy

Received on October 22, 2018. Revised on January 14, 2019. Accepted on January 14, 2019

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This study was supported by a 2018 research from Pusan National University Yangsan Hospital.

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Introduction

Maternal alloimmunization via transfusion, transplantation, or fetomaternal hemorrhage in a previous or current pregnancy is a cause of hemolytic disease of the fetus and newborn (HDFN) [1]. HDFN is a disease, in which maternal red blood cell (RBC) alloantibodies of the Immunoglobulin G (IgG) class are passed actively across the placenta and destroy fetal erythroid cells carrying the antigen involved [1]. The clinical spectrum of the disease varies and includes mild hemolytic anemia, hyperbilirubinemia, hepatomegaly, severe anemia with hydrops, and even death of the fetus, according to the number of RBC antibodies (one vs. multiple) [1-3]. The causative antibodies of severe HDFN, which presents as severe anemia, jaundice, or death in either the fetus or neonate, are anti-D, anti-c, anti-K, anti-C, and anti-E. Other causative antibodies, including those against Rh, Duffy, Kidd, and MNS blood group systems, lead predominantly to anemia or jaundice during the neonatal period [3]. Therefore, an awareness of the prevalence of maternal alloantibodies is important for managing the health of the fetus and neonate. The prevalence of alloantibodies varies in pregnant women, and the expression of RBC antigens differs among ethnicities [4-8]. The prevalence of alloantibodies in pregnant women in Korea was first reported almost 20 years ago [9]; however, there are no reports on the correlation between maternal alloimmunization of RBCs and the health of the fetus and newborn.

This study examined the prevalence and nature of maternal RBC alloimmunization and neonatal outcomes. The fetal and neonatal outcomes of pregnan-

cies with and without RBC antibodies were compared. This study is expected to encourage the establishment of a protocol to evaluate unexpected antibodies during pregnancy.

Materials and Methods

1. Subjects

Pregnant women, who underwent unexpected antibody screening for prenatal testing at the obstetrics and gynecology clinic at Pusan National University Yangsan Hospital from June 2012 to June 2017, were enrolled. This study was approved by the Institutional Review Board of Pusan National University Yangsan Hospital (IRB no. 1708-010-058).

A test group and control group were established to analyze the outcomes of pregnant women with unexpected antibodies. Pregnant women with a positive result were selected as the test group. The control group consisted of age- and obstetric history-matched pregnant women with negative results. The control group were selected randomly among pregnant women who underwent antibody screening from June 2012 to June 2017.

The ABO/Rh (D) type, age, past history of blood transfusion or surgery, obstetric history, and results of unexpected antibody screening of the pregnant women, as well as the ABO/Rh (D) type, gestational age at birth, phototherapy history, bilirubin levels, antiglobulin test results, and mortality of the babies of these women were recorded. For pregnant women displaying alloantibodies initially in the present pregnancy at the authors' center, a serologic phenotyping test was performed for Rhesus, Kidd, Duffy,

and MNS blood group antigens.

ABO/Rh (D) typing and antibody screening were performed using the Ortho AutoVue Innova System (Ortho Clinical Diagnostics, Raritan, NJ, USA). For ABO/Rh (D) typing, 0.8% Affirmagen A1, B Grouping Red Blood Cells (Ortho Clinical Diagnostics), and ABO/Rh Reverse Cassettes (Ortho Clinical Diagnostics) were used. Surgiscreen Reagent sub code D (3%) (Ortho Clinical Diagnostics), which was manufactured as a three-cell panel, including Di^a, and the Polyspecific Anti-Human Globulin Cassette (Ortho Clinical Diagnostics) were used for antibody screening. The antibodies were identified using the ID DiaPanel, ID-DiaPanel P (Bio-Rad, Cressier, Morat, Switzerland), LISS/Coombs card (Bio-Rad Laboratories, Hercules, CA, USA), and NaCl/Enzyme card (Bio-Rad) incorporating the antiglobulin and enzyme methods. Unidentified antibodies were defined as antibodies other than those against the Rh, Kell, Duffy, Kidd, Lewis, P, MNS, Lutheran, and the Xg blood group systems that could be identified using the ID DiaPanel (Bio-Rad) with the LISS/Coombs card and the NaCl/Enzyme card.

Antibody identification was not performed routinely in cases of weakly reactive results or patients lost to follow-up.

2. Other laboratory tests

The direct antiglobulin test [10] was performed using the gel-based Diamed-ID system (Bio-Rad). The total and direct bilirubin levels were measured using the Roche 8000 series Cobas c702 System (Roche Diagnostics, Basel, Switzerland). The reference range of indirect bilirubin differed according to the age of the neonate: 1~3 mg/dL at birth became

5~6 mg/dL between days 2 and 4, and decreased between days 5 and 7 after birth [11].

3. Anti-D prophylaxis

In the authors' hospital, Rh D-negative pregnant women were given anti-D prophylaxis at 28 weeks of pregnancy. When pregnant women experienced vaginal hemorrhage, the physician gave anti-D prophylaxis earlier than 28 weeks.

4. Obstetric follow-up

The guidelines from the Korean Society of Obstetrics and gynecology recommend unexpected antibody screening testing during the prenatal period, including the third trimester of pregnancy [12]. In cases of a positive antibody screening test, the antibody screening test was performed every 72 h if the patient received a blood transfusion. Middle cerebral arterial peak systolic velocity tests were performed on each infant. No participant in this study received an intrauterine transfusion.

5. Statistical analyses

Pearson's chi-square tests were used to compare the categorical variables. A Mann-Whitney U test was used to compare the median (range) value of the continuous variables between the two groups. All statistical analyses were performed using SPSS 18.0 software (SPSS, Inc., Chicago, IL, USA), and *P* values < 0.05 were considered significant.

Results

Overall, 2,493 samples from 1,508 pregnant women were tested within the study period. The median

age of the pregnant women was 33 years (range, 16~46). Of the total samples, 2.36% (59/2,493) showed positive results in the antibody-screening test. After excluding duplicate samples from the same patient, the prevalence of unexpected antibodies was 2.78% (42/1,508). After excluding five cases of passive immunization of anti-D, the actual prevalence of unexpected antibodies was 2.45% (37/1,508).

With the exception of unidentified cases or those not tested, anti-D was the antibody identified most frequently, followed in order by anti-E and anti-Le^a (Table 1). Of all of the Rh D-negative pregnant women, five and four had anti-D because of prophylactic immunization and active immunization. The most common alloantibodies belonged to the Rh system (14/28, 50.0%).

Table 1. Specificities of the red blood cell antibodies in the 37 pregnant women

Blood group system	N	%
Rh		
Anti-D	7	18.9
Anti-E	2	5.4
Anti-E, c	2	5.4
Anti-C, e	1	2.7
Kidd		
Anti-Jk ^a	1	2.7
Lewis		
Anti-Le ^a	5	13.6
MNS		
Anti-M	1	2.7
Others		
Anti-E, Fy ^b	1	2.7
Anti-E, Di ^b	1	2.7
Unidentified	8	21.6
Not tested	8	21.6
Total	37	100.0

Thirty seven pregnant women with unexpected antibodies were assigned to the test group. None of the women in the test group had received a blood transfusion or surgery before the present pregnancy. Thirty-seven pregnant women without unexpected antibodies were enrolled in the control group. Table 2 lists the characteristics of the pregnant women and their neonate or fetus according to the presence of maternal unexpected antibodies. No significant differences in obstetric history (including gravida and para), age, and ABO/blood type were observed between the two groups. Only the survival rate of the current pregnancy was significantly different ($P=0.047$). Perinatal transfusion was more frequent in the test group (14 pregnant women) than in the control group (seven pregnant women), although the difference was not significant ($P=0.071$). All blood products were cross-matched by the Coombs phase and transfused into alloimmunized pregnant women. In the test group, 31 neonates were born alive (six neonates, preterm; 25 neonates, full-term) and six fetuses or newborns were aborted or died at birth. In the control group, 36 neonates were born alive (10 neonates, preterm; 26 neonates, full-term) and one died at birth. No neonates with enzymopathies, hemoglobinopathies, or other forms of liver injury or CMV infection were noted.

Among the six pregnancies in the test group (anti-E [one case], anti-E and anti-c [one case], anti-E and anti-Fyb [one case], unidentified antibody [two cases], and not tested [one case]) that ended in an abortion or stillbirth, two mothers may have experienced an abortion or stillbirth due to systemic lupus erythematosus. The remaining four pregnant women had no specific diseases or no other pre-

Table 2. Characteristics of pregnant women and their neonate or fetus according to the presence of maternal unexpected antibody

	Maternal unexpected antibody		<i>P</i> value
	Positive (test group)	Negative (control group)	
Total number of pregnant women	37	37	
Age (median, range)	34 (25 ~ 44)	33 (25 ~ 43)	0.307
ABO blood group (N, %)			0.985
A/B/AB/O	13 (35.1%)/9 (24.3%)/ 4 (10.8%)/11 (29.7%)	12 (32.4%)/9 (24.3%)/ 5 (13.5%)/11 (29.7%)	
Rh D blood group (N, %)			0.056
Positive/negative	30 (81.1%)/7 (18.9%)	36 (97.3%)/1 (2.7%)	
Packed RBC transfusion before current pregnancy (N, %)			0.115
Yes/no	4 (10.8%)/33 (89.2%)	0 (0.0%)/37 (100.0%)	
Obstetric history			
Gravida (median, range)	2 (1 ~ 5)	2 (1 ~ 6)	0.562
Para (median, range)	0 (0 ~ 2)	0 (0 ~ 2)	0.210
Abortion (median, range)	0 (0 ~ 3)	0 (0 ~ 2)	0.149
Live (median, range)	0 (0 ~ 2)	0 (0 ~ 2)	0.604
Antenatal transfusion history in pregnant women (yes/no)	3 (8.1%)/34 (91.9%)	0 (0.0%)/37 (100.0%)	0.240
Total number of fetuses or neonates	37	37	
Outcome of fetuses or neonates at birth (live/death)	31 (83.8%)/6 (16.2%)	36 (97.3%)/1 (2.7%)	0.047
Total number of live neonates at birth	31	36	
Preterm birth/full-term birth	9 (29.0%)/22 (71.0%)	10 (27.8%)/26 (72.2%)	0.910
Phototherapy (yes/no)	12 (38.7%)/19 (61.3%)	7 (19.4%)/29 (80.6%)	0.081
Total number of neonates with phototherapy	12 (38.7%)	7 (19.4%)	0.081
Times of phototherapy (median, range)	2 (1 ~ 7)	1 (1 ~ 3)	0.536
Peak total bilirubin (median, range)	8.31 (5.2 ~ 14.52)	9.26 (7.24 ~ 12.66)	0.463

sumed cause. In addition, six pregnant women in the test group whose baby was born preterm had anti-D (2 cases), anti-Le^a (2 cases), and an unidentified antibody (one case), and one case did not undergo testing.

Table 3 lists the characteristics of the neonates with the presence of maternal unexpected antibody. One case (case no 22) was presumed to be ABO incompatible between the mother and her neonate. In case number 14, HDFN was suspected, which was confirmed by an elution study on the neonatal RBCs.

Among the eight pregnant women with anti-C or anti-D antibodies, four neonates developed hyperbilirubinemia and received phototherapy. An anti-G test was not performed on anti-C- and anti-D-positive pregnant women. Among the five newborns with maternal anti-Le^a, three developed hyperbilirubinemia. The newborn with maternal anti-Jk^a developed hyperbilirubinemia and had the Jk^a antigen. Of the six pregnant women with anti-E alone or with other alloantibodies, the surviving three neonates did not develop hyperbilirubinemia.

Table 3. Characteristics of the neonates with presence of maternal unexpected antibody

Case number	Mother			Neonate					
	Antibody specificity	ABO blood type	Gestational age at birth	ABO blood type	DAT	Photo-therapy	Total bilirubin (mg/dL)	Hemo-globin (g/dL)	Age (days) at test
1	Anti-D	A (-)	38+5 wks	A (+)	Negative	No	6.68	16.3	2
2	Anti-D	AB (-)	40+0 wks	A (+)	NA	No	5.59	15.2	3
3	Anti-D	O (-)	35+5 wks	B (+)	NA	Yes	NA	16.2	1
4	Anti-D	O (-)	38+4 wks	O (+)	Negative	Yes	7.43	17.1	4
5	Anti-D	A (-)	28+1 wks	O (+)	NA	Yes	7.4	16.1	6
6	Anti-D	A (-)	38+6 wks	A (+)	NA	No	NA	NA	NA
7	Anti-D	A (-)	37+5 wks	O (+)	NA	No	NA	NA	NA
8	Anti-C & e	A (+)	36+0 wks	A (+)	NA	Yes	7.04	16.7	4
9	Anti-E	O (+)	17+5 wks	*	*	*	*	*	*
10	Anti-E	A (+)	37+1 wks	B (+)	NA	No	NA	NA	NA
11	Anti-E & c	A (+)	41+1 wks	A (+)	NA	No	2.83	14.9	1
12	Anti-E & c	O (+)	7+1 wks	*	*	*	*	*	*
13	Anti-E & Fy ^b	B (+)	37+5 wks	*	*	*	*	*	*
14	Anti-E & Di ^b	B (+)	36+2 wks	O (+)	Positive	No	6.27	15.7	15
15	Anti-Jk ^a	A (+)	38+1 wks	AB (+)	NA	Yes	5.2	14.1	3
16	Anti-Le ^a	A (+)	36+4 wks	A (+)	NA	Yes	NA	NA	NA
17	Anti-Le ^a	O (+)	37+4 wks	B (+)	NA	No	7.21	16.5	8
18	Anti-Le ^a	AB (+)	33+4 wks	AB (+)	NA	Yes	8.94	13.9	6
19	Anti-Le ^a	A (+)	36+4 wks	A (+)	NA	Yes	NA	NA	NA
20	Anti-Le ^a	A (+)	37+4 wks	O (+)	NA	No	2.52	17.8	1
21	Anti-M	O (+)	37+3 wks	O (+)	NA	No	NA	NA	NA
22	Unidentified Ab.	O (+)	37+0 wks	A (+)	NA	Yes	7.36	15.1	3
23	Unidentified Ab.	O (+)	37+6 wks	O (+)	NA	No	8.7	16.4	3
24	Unidentified Ab.	A (+)	34+0 wks	B (+)	NA	Yes	14.52	14.7	4
25	Unidentified Ab.	B (+)	34+5 wks	A (+)	NA	Yes	NA	NA	NA
26	Unidentified Ab.	B (+)	37+1 wks	A (+)	NA	No	7.88	13.3	16
27	Unidentified Ab.	B (+)	7+6 wks	*	*	*	*	*	*
28	Unidentified Ab.	AB (+)	37+0 wks	AB (+)	NA	No	NA	NA	NA
29	Unidentified Ab.	AB (+)	22+4 wks	*	*	*	*	*	*
30	Positive, NT	A (+)	38+1 wks	A (+)	NA	Yes	8.55	15.6	5
31	Positive, NT	B (+)	35+0 wks	B (+)	NA	Yes	10.95	17.4	6
32	Positive, NT	B (+)	38+3 wks	O (+)	NA	No	NA	NA	NA
33	Positive, NT	O (+)	37+5 wks	A (+)	NA	No	NA	NA	NA
34	Positive, NT	O (+)	37+3 wks	B (+)	NA	No	NA	NA	NA
35	Positive, NT	B (+)	5+3 wks	*	*	*	*	*	*
36	Positive, NT	B (+)	38+0 wks	A (+)	NA	No	NA	NA	NA
37	Positive, NT	O (+)	38+0 wks	B (+)	NA	No	NA	NA	NA

*The cases of abortion or intra-uterine fetal death.

Abbreviations: Ab., antibody; DAT, direct antiglobulin test; NT, not tested of identification; NA, no data available.

Discussion

HDFN is a preventable cause of fetal morbidity and mortality. Moreover, complications during intra-uterine transfusion, the treatment for HDFN, can lead to death [2]. Early detection of HDFN and monitoring of disease progression are necessary to prevent death of the fetus or neonate. An awareness of the prevalence of maternal alloantibodies is important for managing the health of the fetus and neonate. The frequency of alloimmunization in pregnant women ranges from 0.4% to 4.5% worldwide [4-8,13]. To the best of the authors' knowledge, this is the first report on the prevalence of maternal alloimmunization and the outcomes of fetuses and newborns in Korea. In this study, 2.78% of pregnant women had unexpected antibodies, and the live birth rate of pregnant women with unexpected antibodies was lower than that of the pregnant women without unexpected antibodies. In addition, the prevalence of unexpected antibodies was higher than that of previous studies. This can be attributed to use of three cells for antibody screening and to the positive to weak positive results.

According to the previous studies on alloimmunized pregnant women, the most common clinically significant alloantibodies are those of the Rh system, the frequencies of which are 6.46~58.9% [1,4,7]. Anti-E and anti-C are common alloantibodies among pregnant women [5,13]. In Korea, the prevalence of unexpected antibodies in pregnant women is 1.91% with anti-Lewis and anti-D being the most common [9]. Lee et al. [14], reported that the most frequent types of Rh phenotype discrepancy between pregnant Korean women and their neonates are E and c.

Therefore, anti-E and anti-c could cause severe HDFN in Korea. Moreover, previous studies reported that anti-E alone or in combination with anti-c might cause HDFN and fetal hydrops in Korea [14-16]. In this study, the most common antibodies belonged to the Rh system (anti-D and anti-E combined with anti-c) with the second most common antibodies being anti-Lewis, which is similar to previous studies.

Anti-D has the strongest immunological effect on HDFN. In D-immunized pregnant women, the risk of severe HDFN was approximately 40% [17]. The chance of HDFN increases when anti-D is combined with any other RBC antibody [13]. The hemolytic effects of the anti-c antibody are similar to those of anti-D and are associated with severe HDFN [18]. Anti c induced HDFN results in hydropic stillbirth or perinatal death, or requires treatment, such as intrauterine transfusion or neonatal exchange transfusion [19]. Fetuses and neonates can develop severe HDFN when maternal anti-E is combined with anti c or anti-c alone. HDFN caused by anti-E is usually mild and occurs in neonates [3,5]. A Swedish study reported that alloimmunization with anti-D, anti-E, anti-C, and anti-c was associated with an increased risk of preterm birth and stillbirth, and anti-Le^a was associated with an increased risk of stillbirth [20]. One study on Rh alloimmunization in pregnant women with Rh alloimmunization revealed a significantly higher rate of perinatal mortality (25%), admission at the neonatal intensive care unit, and neonatal transfusion compared to all pregnant women [21]. In the present study, the preterm birth rate did not differ significantly between the test group with unexpected antibodies (19.3%) and the control group

(27.7%). The authors' hospital is a tertiary hospital that can provide intensive care for neonates or any pregnant woman at risk of preterm birth transferred to the hospital. Therefore, the number of preterm births is more than in other hospitals. In the present study, 50% of newborns with maternal anti-D or anti-C developed hyperbilirubinemia and one was a stillbirth. Among six pregnant women with anti-E alone or with other alloantibodies, three (50%) experienced a spontaneous abortion or stillbirth; the surviving neonates did not develop hyperbilirubinemia. Among the two pregnant women who had both anti-E and anti-c, a patient with G4P1A3L1 experienced a spontaneous abortion. Recurrent abortion might have been the result of anti-E with anti-c. Among six newborns with maternal anti-Le^a and anti-Jk^a, four developed hyperbilirubinemia but their mothers had not experienced a spontaneous abortion or stillbirth. Serial screening of unexpected antibodies in pregnant women will be needed if the antibody of the Rh group is revealed as a cause of severe fetal loss.

In most infants, unconjugated hyperbilirubinemia reflects a normal transitional phenomenon and is called physiological jaundice. The bilirubin level of most patients who require phototherapy remains within the physiological range [10,22]. In the present study, however, hyperbilirubinemia occurred earlier in four patients and at higher levels than general physiological jaundice. In these four cases, the effects of maternal RBC alloimmunization might have been overlooked. The possibility of HDFN as a cause cannot be ruled out because the cause of hyperbilirubinemia was not evaluated. Although the bilirubin level was within the level of physiological

jaundice, in the other neonates who received phototherapy, it is possible that the hyperbilirubinemia was caused by mild HDFN. For example, in case seven, the physician did not consider HDFN at all, but the laboratory physician requested the workup for HDFN and the baby was confirmed to have mild HDFN. If a prospective evaluation of neonatal hyperbilirubinemia is performed, the prevalence of HDFN would be determined.

One limitation of this study was the lack of a sufficient workup of neonates with hyperbilirubinemia, including a direct antiglobulin test during treatment in most patients. In addition, the red cell phenotype of the fathers and infants was not determined. Furthermore, the titers of alloantibodies that were isolated were not evaluated. In Korea, the tests for Rh typing and phenotyping for other major antigen systems were not performed routinely. Therefore, the actual prevalence of HDFN could not be determined. A prospective multicenter study with a complete examination of the mothers and neonates is needed.

Conclusion

In conclusion, the prevalence of unexpected antibodies among pregnant Korean women was 2.78%. The most common significant antibodies belonged to the Rh blood group, namely, anti-D, and anti-E combined with anti-c. The death rate of the fetuses was higher in pregnant women with unexpected antibodies than in those without. Significant differences in the neonatal outcomes, including the death rate, prematurity, and hyperbilirubinemia, were observed depending on the specificity of the unexpected antibody. Pregnant women who have an unexpected an-

tibody need to be monitored and the neonates of such women should be evaluated for HDFN.

요 약

배경: 임신부에서 태아와 신생아 용혈성 질환(HDFN)을 일으킬 수 있는 비예기항체의 빈도 및 종류는 연구마다 결과의 차이를 보인다. 태아와 신생아 용혈성 질환의 임상 양상은 비예기항체의 특이성과 정도에 따라 다르다. 이에 저자들은 국내 임신부의 동종면역 발생 빈도와 임상상 및 그에 따른 신생아의 예후를 분석하였다.

방법: 양산부산대학교병원 산부인과에서 산전 검사로 비예기항체 선별 검사를 시행한 임신부를 대상으로 하였다. 비예기항체 선별 검사 결과 양성을 보인 환자군과 연령과 산과력을 맞춘 비예기항체 선별 검사 결과 음성의 임신부로 이루어진 대조군 간의 비예기항체에 따른 임신 예후와 신생아의 예후를 조사하였다.

결과: 비예기항체의 빈도는 2.78% (42/1,508)였다. 동정된 비예기항체 중 항-D가 가장 많이 동정되었고, 그 다음으로 항-E와 항-Le^a 순이었다. 주산기 사망률은 대조군보다 환자군에서 높은 결과를 보였다. 항-C 또는 항-D를 보인 8명의 임신부에서 1명은 사산, 생존 분만 중 4명의 신생아는 고빌리루빈혈증을 보였다. 단일 항체 또는 다른 동종 항체와 동시 동정된 항-E를 보인 6명의 임신부 중 3명에서 자연 유산 또는 사산을 확인했다. 모성 항-Le^a와 항-Jk^a를 보인 6명의 신생아 중 4명에서 고빌리루빈혈증을 확인하였으나, 각각의 산모는 자연 유산 또는 사산 경력은 없었다.

결론: 국내 임신부의 비예기항체의 빈도는 2.78%였다. 비예기항체의 특이성에 따라 주산기 사망률, 조산을 및 신생아 고빌리루빈혈증과 같은 신생아의 예후에 유의한 차이를 보였다.

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