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Original Article

Incidence of Alloantibodies in Transfused Patients in Eastern Taiwan

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Abstract

Objective: The study was conducted to determine the prevalence of red blood cell alloantibodies for transfused patients in the East Taiwanese population.
Materials and Methods: We analyzed the clinical and transfusion records of 15,794 individuals who received transfusions in Hualien Tzu Chi Hospital from 2004 to 2006. Blood samples were subjected to standard blood bank procedures for screening for antibodies.
Results: Of the 15,794 transfused patients, 538 patients (3.39%) were found to have alloantibodies. Among these 538 patients, 333 patients were found to carry alloantibodies at the initial transfusion (2.0%) and 205 (1.3%) patients developed alloantibodies during the transfusion period.
Conclusion: Our data demonstrate that anti-Mi[a] was the most frequently detected alloantibody in the Eastern Taiwanese population, with an incidence (1.5%) that was higher than reported in other Taiwanese populations.
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1. Introduction

Alloimmunity against erythrocyte antigens is one of the major complications of transfusions, particularly in patients who are chronically transfused. This type of sensitization results in difficulty in obtaining compatible blood, reactions to transfusions, hemolysis and occasionally life-threatening adverse events. With the exception of ABO and Rh(D), there is little information about the distribution of blood groups among Chinese people (1). Alloantibody screening is included in routine blood compatibility testing in Taiwan.

Formation of alloantibodies against red blood cells (RBCs) has been well documented in previous studies (2–4). Alloantibodies are directed against the individual's own RBCs, which can result in clinical hemolysis and difficulty in cross-matching blood. Most alloantibodies react with high incidence antigens, causing agglutination and sensitization to RBCs from random donors as well as those of antibody producers. These

circulating humoral antibodies may shorten the duration of RBC survival (5). Patients with alloantibodies may have higher transfusion rates and often require immunosuppressive drugs, splenectomy, or alternative treatments in place of transfusions.

There have been few large-scale studies of erythrocyte alloantibodies in patients from Eastern Taiwan. In this paper, we evaluated the frequency of alloantibodies for patients from the East Taiwanese population.

2. Materials and methods

In Taiwan, pretransfusion testing consists of ABO grouping, antibody screening and major cross matching. From 2004 to 2006, antibody screening and cross-matching were performed on 15,794 consecutive patients in Hualien Tzu Chi Hospital using the manual hexadimethrine bromide method. We analyzed transfusion records of these patients for this study. We identified all antibodies from positive antibody screening tests or incompatible cross-matches and calculated the incidence of clinically significant alloantibodies. The χ^2 test was performed to test for gender and age-group homogeneity in this group. The level of significance was set at 0.05 for each test. All analyses were carried out using SPSS version 13.0 (SPSS Inc., Chicago, IL, USA).

3. Results

A total of 15,794 transfused patients were included in our study. The clinically significant alloantibodies identified in our blood bank over the 3-year period are shown in Table 1. A total of 538 patients (538/15,794, 3.39%) were found to have alloantibodies. Among this group of patients, 329 patients (2.0%) were found to

Table 1 — Alloantibodies detected in patients transfused at Hualien Tzu Chi Hospital from 2004 to 2006

Alloantibody				First (*n*=329)		Secondary (*n*=212)		Total (*n*=538)	
				n	%	*n*	%	*n*	%
c				3	0.91	1	0.47	4	0.74
e				6	1.82	5	2.36	11	2.04
C				1	0.30	0	0.00	1	0.19
D				3	0.91	0	0.00	3	0.56
Dia				3	0.91	3	1.42	6	1.12
E				42	12.77	42	19.81	84	15.61
I				0	0.00	2	0.94	2	0.37
JKa				2	0.61	3	1.42	5	0.93
JKb				0	0.00	1	0.47	1	0.19
Lea				24	7.29	20	9.43	44	8.18
Leb				3	0.91	4	1.89	7	1.30
M				16	4.86	7	3.30	23	4.28
Mi^a				181	55.02	58	27.36	239	44.42
P1				10	3.04	13	6.13	23	4.28
e	C			1	0.30	4	1.89	5	0.93
C	e	Mi^a		1	0.30	0	0.00	1	0.19
E	c			20	6.08	19	8.96	39	7.25
E	c	JKa		0	0.00	1	0.47	1	0.19
E	c	Mi^a		4	1.22	2	0.94	6	1.12
E	c	Mi^a	E	0	0.00	1	0.47	1	0.19
E	c	Mi^a	autoAb	0	0.00	1	0.47	1	0.19
E	c	Mi^a	P1	0	0.00	1	0.47	1	0.19
E	c	S	Fyb	1	0.30	1	0.47	1	0.19
E	JKa			0	0.00	1	0.47	1	0.19
E	JKb			1	0.30	1	0.47	1	0.19
E	Lea			0	0.00	1	0.47	1	0.19
E	M			0	0.00	1	0.47	1	0.19
E	P1			0	0.00	1	0.47	1	0.19
E	Mi^a			3	0.91	9	4.25	12	2.23
E	Mi^a	Dia		0	0.00	1	0.47	1	0.19
E	Mi^a	M		0	0.00	1	0.47	1	0.19
E	Mi^a	autoAb		0	0.00	1	0.47	1	0.19
Lea	Dia			1	0.30	1	0.47	1	0.19
Lea	Leb			1	0.30	2	0.94	3	0.56
Lea	P1			0	0.00	1	0.47	1	0.19
Mi^a	N			0	0.00	2	0.94	2	0.37
Mi^a	JKa			1	0.30	0	0.00	1	0.19
autoAb	E			1	0.30	0	0.00	1	0.19

Table 2 — Demographic data of 538 patients

Demographic data	Patients, *n* (%)	*p**
Gender		0.49
Male	277 (51.49)	
Female	261 (48.51)	
Age (yr)		<0.001
1–20	11 (2.04)	
21–40	66 (12.27)	
41–60	177 (32.9)	
61–80	234 (43.49)	
81–100	50 (9.3)	

*Obtained using the χ^2 test of homogeneity.

Table 3 — Gender and age differences in the most common alloantibody types at first transfusion

	anti-E (*n*=42)	anti-Lea (*n*=24)	anti-Mi^a (*n*=181)	anti-E/c (*n*=20)
Gender				
Male	20	13	87	13
Female	22	11	94	7
*p**	0.758	0.683	0.603	0.18
Age (yr)				
1–20	1	0	3	0
21–40	3	5	19	3
41–60	15	10	63	10
61–80	19	7	77	6
81–100	4	2	19	1
*p**	<0.001	0.129	<0.001	0.027

*Obtained using the χ^2 test of homogeneity. Anti-E/c=detection of both anti-E and anti-(c) antibodies.

carry alloantibodies at the time of initial transfusion. A total of 212 patients (1.3%) subsequently developed alloantibodies during the transfusion period, indicating the frequency of recent alloimmunization. During the initial transfusion (Table 1), the anti-Mi^a alloantibody was observed most frequently (55.02%). The least common alloantibody, anti-C, was found in only one person. Anti-I and anti-JKb alloantibodies were not observed. In patients with multiple alloantibodies, anti-E and anti-(c) were most frequently detected.

With alloimmunization secondary to transfusion (Table 1), anti-Mi^a was observed most frequently (27.36%). However, the frequency of the alloantibody anti-E was increased to 19.81%. The least common types were anti-(c) and anti-JKb. In patients with multiple alloantibodies, anti-E and anti-(c) were observed most frequently (8.96%).

Demographic variables, including gender and age group, are shown in Table 2. Gender distribution was homogeneous, with no significant differences in the frequency of the most common alloantibody types between males and females at the time of initial transfusion (Table 3). However, the frequency of alloantibody detection was significantly different between age groups. In particular, alloantibody frequency in patients aged 61–80 years (43.49%) was noticeably higher than in the other age groups. To illustrate this, we have listed in Table 3 the frequencies of four common alloantibody types (anti-E, anti-Lea, anti-Mi^a, and the most frequent multiple alloantibody combination of anti-E and -(c)) according to gender and age group. Only the anti-Lea alloantibody was not significantly different among the five age groups. For the second transfusion assessment, the frequency of anti-Mi^a detection in males was greater than that in females, while the other three common alloantibody types were homogeneous (Table 4). Interestingly, the distribution of anti-E and anti-(c) was also homogeneous among the five age groups.

Table 4 — Gender and age differences in the most common alloantibody types at second transfusion

	anti-E (*n*=42)	anti-Lea (*n*=20)	anti-Mi^a (*n*=58)	anti-E/c (*n*=19)
Gender				
Male	20	14	38	7
Female	22	6	20	12
*p**	0.758	0.074	0.018	0.251
Age (yr)				
1–20	1	1	2	1
21–40	5	3	8	3
41–60	13	4	15	6
61–80	24	10	28	5
81–100	2	2	5	4
*p**	<0.001	0.014	<0.001	0.42

*Obtained using the χ^2 test of homogeneity. Anti-E/c=detection of both anti-E and anti-(c) antibodies.

4. Discussion

In the past, routine pretransfusion testing in Taiwan included only ABO grouping and room-temperature major and minor cross-matches, mostly done by a slide method. Overt hemolytic transfusion reactions were almost exclusively a result of ABO mismatches. Even though antibody screening has been introduced in recent years as an essential part of compatibility testing, clinically significant alloantibodies were encountered comparatively more frequently, ranging from 3.55% in the East Taiwanese population to 2.1% at Mackay Memorial Hospital (6). In our investigation, at both the initial and second transfusion assessments a single alloantibody was found most frequently. This includes 239 cases with anti-Mi^a of 538 patients with alloantibodies. Therefore the frequency of anti-Mi^a among transfused patients was 1.5% (239/15,794), higher than the 1.2% noted at Mackay Memorial Hospital (6). The significance of this finding is unclear given the limited data on the transfusion recipients in the study, including data on the heterogeneity of ethnicity, multiple transfusions, and frequency of different diseases. Anti-Mi^a has been observed with greater frequency in children than in adults (7). This age bias has

been postulated to be due to bacterial infections within the pediatric age range.

The term anti-Mi^a is used throughout this report to describe those antibodies in our patients' sera that react with antibody-screening cells of the Mi III phenotype. Anti-Mi^a appears to be an alloantibody of potential clinical significance in Taiwan and, therefore, it may be important that Mi III RBCs are included in the antibody screening cells used in blood banks in Taiwan. In fact, this has been the situation since July 1990. Because patients expressing anti-Mi^a may have a history of blood transfusion or pregnancy, anti-Mi^a may occur either naturally or as a result of immunization in these patients.

In our study, the second most common single alloantibody was anti-E (0.53%, 84/15,794). Before routine screening for anti-Mi^a was instituted, the frequency of alloantibodies of potential clinical significance that were detected among Chinese patients at Mackay Memorial Hospital between 1984 and 1987 was found to be 0.146%, with anti-E being the most common single specificity [1,8].

Among patients with multiple alloantibodies, anti-E and anti-(c) were found to be the most common in primary and secondary alloimmunization. This result is similar to the results of other studies [1,9]. The opportunity for immunization to both E and c is very similar in both Chinese and Caucasians, although the most common alloantibodies, anti-E and anti-(c), occur much less frequently among Chinese than in Caucasians. Therefore, we hypothesize that the reaction to red cell antigenic stimulus is worse amongst Chinese patients than amongst Caucasians.

In our study, patient gender did not impact the frequencies of alloantibodies against red blood cell antigens. The greater prevalence of alloimmunization among females, with a male:female ratio of 1:2.7, is similar to the 1:2 ratio reported by some [10,11], but not all [12,13], studies. Possible explanations for the increased antibody prevalence in females may include previous exposure through pregnancy, greater immune response in women, and greater exposure of women through transfusion.

However, at the second transfusion, anti-Mi^a was more frequent in males than in females in this study. The reason for this difference is not clear. Blumberg et al [11] reported a male:female alloimmunization ratio of 1:2 before transfusion, but they also reported a 2:1 ratio for the development of new antibodies during transfusion. These findings suggest that an enhanced immune response is not the cause of the observed female predominance, because the frequency of alloimmunization after transfusion was equivalent [12,13] or greater [11] in males.

When age was taken into account, there were significant differences in the frequency of alloantibody detection. Specifically, the frequency of alloantibodies in patients aged 61–80 years (43.49%) was higher than that of other groups. When considering the common alloantibodies (anti-E, anti-Lea, anti-Mi^a) and one multiple alloantibody (anti-E and anti-(c)), transfusion recipient age was a dominant factor in the initial and secondary transfusion ($p<0.001$), with the exception of anti-Lea and multiple alloantibody detection. This interesting observation in our study may be related to greater exposure and immunization with age.

In summary, this study shows that red blood cell alloantibodies are a frequent finding amongst patients in the East Taiwanese population. Several factors might have contributed to this finding, including the heterogeneity of the population, increased frequency of transfusion, and population exposure to different diseases. It should be noted that potential selection bias may influence the calculations and results discussed above. For these reasons, further investigation is required in order to prevent alloimmunization in patients requiring chronic transfusion therapy.

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