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Alloimmunization and Erythrocyte Autoimmunization In Transfusion Dependent Thalassemic Patients

Thesis

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Introduction

The thalassemias are a group of anemias that result from inherited defects in the production of hemoglobin. The thalassemias are among the most common genetic disorders worldwide, occurring more frequently in the Mediterranean region, the Indian subcontinent, Southeast Asia, and West Africa. Ineffective bone marrow erythropoiesis and excessive red blood cell hemolysis together account for the anemia. ***(Alain., 2007).***

Since reticulocytes manufacture equimolecular quantities of alpha and beta chains, mature erythrocytes contain essentially equimolecular amounts of each chain. Patients with thalassemia do not produce enough hemoglobin (Hb) A ($\alpha 2\beta 2$) because their cells cannot manufacture either the alpha or beta polypeptide chain of human hemoglobin. Alpha-thalassemia depresses only the production of the alpha chains, and beta-thalassemia depresses only the production of the beta chains. Clinically, both alpha- and beta-thalassemia may occur in the major (homozygous), intermediate, and minor (heterozygous) genetic forms and also can interact with the presence of abnormal hemoglobins in the same individual. ***(Alain., 2007).***

The globin chain that is produced in excess is responsible for the ineffective erythropoiesis and shortened red blood cell (RBC) survival. In the absence of stem cell transplantation the disease is treated by life long red cell transfusion to keep the hemoglobin level between 9–11.5 g/dL. Regular blood transfusions are essential to maintain growth and development during childhood and also to sustain good quality of life durifng adulthood. ***(Shamsian., 2008).***

However, disease- and treatment-related complications in these patients progress over time, causing severe morbidity and shortened life expectancy. Stem cell transplantation still remains the only cure currently available for patients with thalassemia ***(Javid et al., 2005).***

Transfusion therapy leads to excess iron accumulation in many organs resulting in tissue damage. Therefore, iron chelation is essential in the management of this otherwise fatal disease ***(Gardenghi et al., 2007).***

Iron-induced organ degeneration is the main factor of mortality in patients with thalassemia major ***(Vassilis et al., 2005).***

β-thalassemia intermedia, in which a larger amount of β-globin chains are synthesized, the clinical picture is milder and the patients do not require frequent transfusions.

However, progressive iron overload still occurs due to increased gastrointestinal (GI) iron absorption. Studies in thalassemic patients showed that the rate of iron uptake from the GI tract is approximately 3 to 4 times greater than normal ***(Gardenghi, et al., 2007).***

Alloimmunization to erythrocyte antigens is one of the major complications of transfusions, particularly in patients who are chronically transfused. This type of sensitization results in difficulty obtaining compatible blood, transfusion reactions, haemolysis and occasionally life-threatening events ***(Wang et al., 2005).***

The factors for alloimmunization are complex and involve at least 3 main contributing elements: the RBC antigenic difference between the donor and the recipient, the recipient's immune status, and the immunomodulatory effect of the allogenic blood transfusions on the recipient's immune system. ***(Shamsia, 2008).***

Some antibodies are known to be clinically significant (i.e. cause haemolysis) such as anti –A, B, D and Kell. Others are usually not considered clinically significant, such as anti –Lea ***(Meny, 2004).***

Conclusion

The present study revealed that alloimmunization to red blood cell antigens are frequent finding and quite relevant among Egyptian transfusion-dependent thalassemic patients.

The most frequent Antibodies detected were Anti-Kell and Anti-E. The majority of alloantibodies detected in the current study were clinically significant.

Autoimmunization was not a frequent finding in our study.

There are several factors that might have contributed to this problem:

- Multiple allogenic blood exposure with majority of patients was transfused with blood matched for ABO&D antigens only.
- No phenotypically matched donors except for limited number of patients.
- Transfusion of non leukodepleted red blood cells in most instances or post storage leukodepleted red blood cells.
- The recipient's immune status.

Data Table

Name	No.	Age	Sex	Diagnosis	Consanguinity	Time interval from start of Tx.	Frequency of Tx.	Spleen presence&age of removal	Exposure to non leucodepleted blood	Thalassemic features	Blood Groub	Phenotyping	Previous Ab. Screen	Present Ab. Screen	Ab. Identification	Ab. Number	HBVsAg	HCV Ab.	auto
Wael M. Galal	1	>20	male	Thalassemia Intermedia	negative	>10	<12units/yr	<10	>10 yr.	y	A positive	R1r, Kell negative	negative	positive	anti-Jka , anti-Fya	2	negative	positive	no
Heba Ramadan Mohamed	2	>20	female	Thalassemia Major	negative	>10	>=12	splenomegaly	<5	y	B positive	R1r, Kell negative	negative	negative		0	negative	positive	no
Noha Kamel A Aziz	3	>=10-20	female	Thalassemia Major	negative	>10	>=12	splenomegaly	0	n	B positive		negative	negative		0	negative	negative	no
Eman Mohamed Said	4	>=10-20	female	Thalassemia Major	positive	>10	>=12	_>=10-20	>=5-10	y	B positive	R1r, Kell negative	negative	negative		0	negative	positive	no
David Remon Kamel	5	<10	male	Thalassemia Major	positive	>=5-10	>=12	splenomegaly	0	n	A positive		negative	negative		0	negative	positive	no
Ahmed Ramadan Mohamed	6	>20	male	Thalassemia Major	negative	>10	>=12	_>=10-20	>10 yr.	y	B positive		negative	negative		0	negative	positive	no
Marawan Magdi Hesan	7	<10	male	Thalassemia Major	negative	<5	>=12	splenomegaly	0	n	A positive	R1r, Kell negative	negative	positive	anti-E	1	negative	negative	no
Mohamed Moharam ali	8	>20	male	Thalassemia Major	negative	>10	>=12	_>=10-20	>10 yr.	y	O positive	R0r	negative	negative		0	negative	positive	no
Basel Ahmed Mohamed	9	<10	male	Thalassemia Major	negative	<5	>=12	<10	0	n	A positive	R1r, Kell negative	negative	positive	anti-Kell	1	negative	negative	no
miar Hosam Eldin Mohamed	10	>=10-20	female	Thalassemia Major	positive	>10	>=12	<10	0	y	O positive		negative	negative		0	negative	positive	no
Tarek Mostafa Elgerahi	11	>20	male	Thalassemia Intermedia	negative	>10	<12units/yr	_>=10-20	<5	y	A positive	Rzr, Kell negative	negative	positive	anti-E	1	negative	negative	no
Nada Alaa Kamal	12	<10	female	Thalassemia Major	negative	>=5-10	>=12	splenomegaly	0	n	AB positive		negative	negative		0	negative	negative	no
Abd Elrahman Atef Mohamed	13	<10	male	Thalassemia Major	negative	>=5-10	>=12	<10	0	n	A positive		negative	positive	anti-D, anti-C	2	negative	positive	no
Abd Elwahab Alaa Kamal	14	<10	male	Thalassemia Major	negative	>=5-10	<12units/yr	splenomegaly	<5	n	B positive	R1r, Kell negative	negative	positive	anti-S, anti-M	2	negative	negative	no
Habeba Waled Ahmed	15	<10	female	Thalassemia Major	positive	<5	>=12	splenomegaly	0	n	O positive	R1r, Kell negative	negative	negative		0	negative	negative	no
Gehan Khalil Elsayed	16	>=10-20	female	Thalassemia Major	negative	>10	>=12	<10	>=5-10	y	AB positive		negative	negative		0	negative	positive	no
Norhan Salah Mohamed	17	>=10-20	female	Thalassemia Major	positive	>10	>=12	<10	<5	y	B positive	R1R1, Kell negative	negative	negative		0	negative	negative	no
Gehan Ali Abd Elkader	18	>20	female	Thalassemia Major	negative	>10	<12units/yr	_>=10-20	>10 yr.	n	B positive	Rzr, Kell negative	negative	positive	anti-Kell, anti-S, anti-Fya, anti-Lea	4	negative	positive	no
Shimaa Hamdi Said	19	<10	female	Thalassemia Major	positive	<5	>=12	splenomegaly	0	n	B positive		negative	negative		0	negative	negative	no
Ghada Fouad Ahmed	20	>=10-20	female	Thalassemia Major	positive	>10	>=12	<10	>10 yr.	y	A positive		negative	negative		0	negative	positive	no
Ahmed Fouad Ahmed	21	>20	male	Thalassemia Major	positive	>10	>=12	_>=10-20	>10 yr.	y	A positive		negative	negative		0	negative	positive	no
Hamada Abdallah Hasan	22	>20	male	Thalassemia Major	negative	>10	>=12	_>=10-20	>10 yr.	y	O positive		negative	negative		0	negative	positive	no
Mona Shokri gerges	23	>20	female	Thalassemia Intermedia	negative	>10	<12units/yr	splenomegaly	>10 yr.	y	A positive	R1r, Kell negative	negative	negative		0	negative	positive	no
Said Mohamed Sayed	24	>20	male	Thalassemia Intermedia	negative	>10	<12units/yr	splenomegaly	>10 yr.	y	A positive	R1R1, Kell negative	negative	negative		0	negative	positive	no
Maria Amir Welson	25	>=10-20	female	Thalassemia Major	negative	>10	>=12	splenomegaly	0	n	A positive		negative	negative		0	negative	negative	no
Marina Amir Welson	26	>=10-20	female	Thalassemia Major	negative	>10	>=12	splenomegaly	0	n	AB positive	R1r, Kell negative	negative	positive	anti-E	1	negative	negative	no
Marwa Magdi Elsayed	27	>20	female	Thalassemia Intermedia	negative	>10	<12units/yr	splenomegaly	<5	n	O positive	R1r, Kell negative	negative	positive	anti-Kell	1	negative	negative	no
Abd Elrahman Samir Biomy	28	<10	female	Thalassemia Major	positive	<5	>=12	splenomegaly	0	n	A positive		negative	negative		0	negative	negative	no
Heba Beshara Khalil	29	<10	female	Thalassemia Major	negative	>=5-10	>=12	splenomegaly	<5	n	O positive		negative	positive	anti-E, anti-Kell	2	negative	negative	no
Fatma Sabry Mohamed	30	>20	female	Thalassemia Major	negative	>10	>=12	_>=10-20	>10 yr.	y	B positive	R0r, Kell negative	negative	negative		0	negative	negative	no
Fatma Ibrahim Mohamed	31	<10	female	Thalassemia Major	negative	<5	>=12	splenomegaly	0	n	O positive	R1r, Kell negative	negative	negative		0	negative	negative	no
Nivin Twfik Khalaf	32	>20	female	Thalassemia Major	negative	>10	>=12	_>=10-20	>10 yr.	n	B positive		negative	negative		0	negative	positive	no
Omar mostafa mohamed	33	>20	male	Thalassemia Intermedia	negative	>10	<12units/yr	>20	<5	y	O positive		negative	negative		0	negative	positive	no
Omnia Hesan Mohamed	34	<10	female	Thalassemia Major	negative	>=5-10	>=12	<10	<5	y	A positive		negative	negative		0	negative	negative	no
Radwa Adel Ragheb	35	>=10-20	female	Thalassemia Major	positive	>10	>=12	_>=10-20	>=5-10	y	B positive	R1R1, Kell negative	negative	negative		0	negative	positive	no
Fawzia Mohamed Mostafa	36	>20	female	Thalassemia Major	negative	>10	>=12	>20	>10 yr.	y	B Negative	r r, Kell negative	negative	negative		0	negative	positive	no
Helal Masoud Abo Bakr	37	>=10-20	male	Thalassemia Major	negative	>10	>=12	<10	<5	y	O positive		negative	negative		0	negative	negative	no
Amr Ahmed Kamel	38	>20	male	Thalassemia Major	negative	>10	>=12	_>=10-20	>10 yr.	y	AB positive		negative	negative		0	negative	positive	no
Amal Imam Rabee	39	>20	female	Thalassemia Intermedia	negative	<5	<12units/yr	splenomegaly	0	n	B positive	R0r, Kell negative	negative	negative		0	negative	negative	nu
Magdi Hasan Mohamed	40	>20	male	Thalassemia Major	negative	>10	>=12	_>=10-20	>10 yr.	y	B positive	Rzr, Kell negative	negative	positive	anti-Kell	1	negative	positive	no
Amira Tados Aziz	41	>20	female	Thalassemia Intermedia	negative	>10	<12units/yr	_>=10-20	>10 yr.	y	B positive		negative	negative		0	negative	positive	no
Marawan Magdi Husin	42	<10	male	Thalassemia Major	negative	>=5-10	>=12	splenomegaly	0	n	A positive		negative	positive	anti-E	1	negative	negative	no
Omnia Sherif Mosleh	43	<10	female	Thalassemia Major	negative	>=5-10	>=12	<10	<5	n	A positive	Rzr, Kell negative	negative	negative		0	negative	negative	no
Mahmod Eid Hasan	44	>20	male	Thalassemia Major	negative	>10	>=12	_>=10-20	>10 yr.	y	O positive	R0r, Kell negative	negative	positive	antifya-antiE	1	negative	positive	no
Asmaa Kamal Mohamed	45	>=10-20	female	Thalassemia Major	negative	>10	>=12	splenomegaly	>=5-10	y	O positive		negative	negative		0	negative	positive	no
Abd Elkhalek Abd Elati Abbas	46	>20	male	Thalassemia Major	positive	>10	>=12	_>=10-20	>10 yr.	y	A positive		negative	negative		0	negative	positive	no
Tarek Elsayed Ahmed	47	>20	male	Thalassemia Major	positive	>10	>=12	>20	>10 yr.	y	B positive	R1R1, Kell negative	negative	positive	anti-E	1	negative	positive	no
Amir Mostafa Kamel	48	<10	male	Thalassemia Intermedia	negative	<5	<12units/yr	splenomegaly	<5	n	B positive		negative	negative		0	negative	negative	no
Abd Elrahman Ali Esmail	49	>20	male	Thalassemia Intermedia	negative	>10	<12units/yr	splenomegaly	>10 yr.	y	A negative	r r, Kell negative	negative	positive			negative	positive	no
Walid Mohamed Said	50	>20	male	Thalassemia Major	negative	>10	>=12	_>=10-20	>10 yr.	y	B positive		negative	negative		0	negative	positive	no
Aliaa Abdallh Mohamed	51	>20	female	Thalassemia Major	negative	>10	>=12	_>=10-20	>10 yr.	y	B positive		negative	negative		0	negative	positive	no
Husin Reda Zaki	52	<10	male	Thalassemia Major	negative	>=5-10	>=12	splenomegaly	<5	y	AB positive		negative	negative		0	negative	negative	no
Mohamed Salah Kamal	53	<10	male	Thalassemia Major	negative	<5	>=12	splenomegaly	0	n	O positive	R1r, Kell negative	negative	negative		0	negative	negative	no
Adham Hosam Hasan	54	<10	male	Thalassemia Major	negative	<5	>=12	splenomegaly	0	n	B positive		negative	negative		0	negative	negative	no
Maia Hamde Mahmod	55	<10	female	Thalassemia Major	negative	<5	>=12	splenomegaly	0	n	A positive	R1r, Kell negative	negative	negative		0	negative	negative	no
Alia Said Mohamed	56	>20	female	Thalassemia Major	negative	>10	>=12	_>=10-20	>10 yr.	y	O positive	R1R1, Kell negative	negative	positive	anti-E, anti-Kell, anti-Jka,anti-Yka	4	negative	positive	no
Naema Zaghlol Hesan	57	<10	female	Thalassemia Major	negative	>=5-10	>=12	splenomegaly	0	y	A positive		negative	negative		0	negative	negative	no
Hany Eshak Ebrahem Sedrak	58	>20	male	Thalassemia Intermedia	negative	>10	<12units/yr	>20	>10 yr.	y	A positive	R1r, Kell negative	negative	positive	anti-E, anti-Kell	2	negative	positive	no
Nesren Hamde Mahmod	59	>20	female	Thalassemia Intermedia	negative	>10	<12units/yr	splenomegaly	0	y	A positive		negative	negative		0	negative	positive	no
Yehia Goma abdelaziz	60	>20	male	Thalassemia Major	negative	>10	>=12	>20	>10 yr.	y	B positive		negative	negative		0	negative	positive	no
Salwa Mohamed Roshde	61	>20	female	Thalassemia Intermedia	negative	>10	<12units/yr	splenomegaly	0	n	AB positive	R1R1, Kell negative	negative	positive	anti-E,anti-c,anti-Jkb	2	negative	positive	no
Mayar Hosam Eldin Mohamed	62	>=10-20	female	Thalassemia Major	positive	>=5-10	>=12	<10	0	n	O positive		negative	negative		0	negative	positive	no
Fawzi Shokri Nagib	63	>=10-20	male	Thalassemia Major	positive	>10	>=12	<10	>=5-10	y	A negative		negative	positive	anti-D	1	negative	negative	no
Ayat Sobhi Fouad	64	<10	female	Thalassemia Major	negative	>=5-10	>=12	splenomegaly	0	n	O positive		negative	negative		0	negative	negative	no
Shimaa Sobhi Fouad	65	>=10-20	female	Thalassemia Major	negative	>=5-10	>=12	splenomegaly	<5	n	O positive		negative	negative		0	negative	negative	no
Eman Husin Mohamed	66	>=10-20	female	Thalassemia Major	negative	>10	>=12	splenomegaly	>=5-10	y	A positive		negative	negative		0	negative	positive	no
Hend Hamdi Abdelrehim	67	>20	female	Thalassemia Intermedia	negative	>10	<12units/yr	splenomegaly	>10 yr.	n	B positive	R0r, Kell negative	negative	negative		0	negative	positive	no
Esam Said Abdelaziz	68	>20	male	Thalassemia Intermedia	negative	>10	<12units/yr	splenomegaly	>10 yr.	y	O positive	R1R1, Kell negative	negative	positive	anti-C, anti-Kell	2	negative	positive	no
Shimaa Adel	69	>=10-20	female	Thalassemia Major	negative	>10	>=12	splenomegaly	>=5-10	n	O positive	R1r, Kell negative	negative	negative		0	negative	negative	no
Momen Samir Abdelrehim	70	<10	male	Thalassemia Major	negative	<5	>=12	splenomegaly	0	n	A positive	R1R1, Kell negative	negative	positive	anti-Leb	1	negative	negative	no
Ihab Ahmed Abdallh	71	>20	male	Thalassemia Major	negative	>10	>=12	>20	>10 yr.	y	O positive	R1r, Kell negative	positive	positive	anti-E, anti-Kell	2	negative	positive	yes
Shimaa Mohamed Abdelmonem	72	>=10-20	female	Thalassemia Major	negative	>10	>=12	splenomegaly	<5	y	A positive		negative	negative		0	negative	negative	no
Fatma Kamal Ali	73	>20	female	Thalassemia Intermedia	negative	>10	<12units/yr	splenomegaly	>10 yr.	n	O positive		negative	positive	anti-c	1	negative	positive	no
Negm eldin Abdelrehim Mohamed	74	>20	male	Thalassemia Major	negative	>10	>=12	>20	>10 yr.	y	A positive		negative	negative		0	negative	positive	no
Doaa Abdelrahman Mohamed	75	>=10-20	female	Thalassemia Major	negative	>10	>=12	<10	<5	y	A positive	R1r, Kell negative	negative	positive	anti-Lua antikell	1	negative	positive	no
Tamer Mansy Elsayed	76	>20	male	Thalassemia Major	negative	>10	>=12	<10	>10 yr.	y	O Negative	r r, Kell negative	negative	positive	anti-D,C,E,Kell,Jkb,S	6	negative	positive	no
Mohamed Ahmed Rashed	77	<10	male	Thalassemia Intermedia	negative	>=5-10	<12units/yr	splenomegaly	0	y	O Negative		negative	negative		0	negative	negative	no
Fayza Mohamed Gad	78	>20	female	Thalassemia Intermedia	negative	>10	<12units/yr	_>=10-20	>10 yr.	y	A positive		negative	negative		0	negative	positive	no
Mostafa Abdelhi Mohamed	79	>=10-20	male	Thalassemia Major	positive	>10	>=12	_>=10-20	<5	y	O positive		negative	negative		0	negative	positive	no
Hanan Elsayed Ahmed	80	>20	female	Thalassemia Major	positive	>10	>=12	splenomegaly	>10 yr.	y	A positive		negative	negative		0	negative	positive	no
Mohamed Ahmed Mohamed	81	<10	male	Thalassemia Intermedia	negative	<5	<12units/yr	splenomegaly	0	n	A positive		negative	negative		0	negative	negative	no
marowa aid said	82	<10	female	Thalassemia Intermedia	positive	<5	<12units/yr	splenomegaly	<10	Y	A positive		negative	negative		0	negative	negative	no
Mohmed esam Eldin	83	<=10	male	Thalassemia Major	positive	<5	>=12	<10	<10	N	Opos	R1R1 Kell	positive	positive	antic,antiE	2	positive	negative	no
Pols Eskandre	84	<10	male	Thalassemia Major	positive	<5	>=12	splenomegaly	<5	N	AB pos	Rzr Kell negative	negative	negative		0	negative	negative	no
Abd Elfatah Selim	85	<10	male	Thalassemia Major	positive	<5	<=12	NO	0	n	B pos	R1R1 Kell	negative	negative		0	negative	negative	no
Ahmed Naser Ali	86	<10	male	Thalassemia Major	negative	<5	<12	splenomegaly	<5	n	O positive		negative	positive	Anti Kell	1	positive	negative	no
Marim Abd Elrahman	87	<10	female	Thalassemia Major	positive	<5	<=12	NO	0	n	O positive		negative	negative		0	negative	negative	no
fady tharwathenry	88	<10	male	Thalassemia Major	positive	<5	<=12	NO	0	n	O Negativ	rr Kell neg	negative	negative		0	negative	negative	no
Mostafa ahmed korani	89	<10	MALE	Thalassemia Major	positive	>5	>12		>5	n	B pos		negative	negative		0	positive	positive	no
Manal Ahmed Korany	90	>10	Female	Thalassemia Major	positive	>10	>12	splenoctomy	>10	n	B pos		negative	negative		0	negative	negative	no
Ahmed Mohamed A.Elshafy	91	<10	Male	Thalassemia Major	positive		>12	splenomegaly	0	n	B pos		negative	negative		0	negative	negative	no
Fatma Yasser Hamdy	92	<10	female	Thalassemia Major	positive	>5	>12	splenomegaly	<5	n	B pos		negative	negative		0	negative	negative	no
Gody Khaled	93	<10	female	Thalassemia Major	negative	>5	<12	no	<5	n	O positive		negative	negative		0	negative	negative	no
AMNA Said mohamed	94	>20	female	Thalassemia Intermedia	positive	>10	<12	>10	>10	n	opos	R2r Kell Negative	positive	positive	antiC ,Kell,s,Fyb,M	5	positive	negative	no
amr asam	95	<5	male	Thalassemia Major	negative	<5	>12		<5	n	A POS								

DISCUSSION

β-thalassemia major is a congenital hemolytic anemia caused by defects in β-globin chain synthesis. The globin chain that is produced in excess is responsible for the ineffective erythropoiesis and shortened red blood cell (RBC) survival. In the absence of stem cell transplantation the disease is treated by life long red cell transfusion to keep the hemoglobin level between 9–11.5 g/dL. Regular blood transfusions are essential to maintain growth and development during childhood and also to sustain good quality of life during adulthood ***(Shamsian et al., 2008)***

The development of anti red blood cell antibodies (Alloantibodies and /or Autoantibodies) can significantly complicate transfusion therapy ***(Sylvia et al., 2004).***

Some antibodies are known to be clinically significant (i.e. cause haemolysis) such as anti –A, B, D and Kell. Others are usually not considered clinically significant, such as anti –Lea (***Meny., 2004).***

The identification of alloantibodies in the recipient's serum makes further transfusions safer as compatible blood can be provided. Especially for patients prone to receive multiple transfusions, compatibility for red cell antigens must include ABO, Rh as well as minor antigens, although the majority of

haemolytic transfusion reactions are due to a limited number of alloantibodies. Antibodies against high-frequency antigens can hinder obtaining suitable blood units and a lack of phenotypic compatibility between donor and recipient blood may result in potential life-threatening complications. ***(Francisco and Santos., 2007).***

It is well known that alloimmunization to red blood cell antigens resulting from the genetic disparity between donor and recipient is one of the risks of blood transfusion that result in resistance to transfusion therapy. The risk depends on the recipient exposure to the foreign antigen and its immunogenicity. Immunization may be influenced by the number and frequency of the transfusions as well as the recipient's sex, age and underlying disease ***(Young et al., 2004)***.

In the present study, a total of 95 regularly transfused thalassemic patients were examined for the presence of red blood cell alloantibodies.

Twenty seven patients (28.4%) of the total number of patients (95) were found to have alloantibodies to red blood cells (table 14), of these patients, 14 (14.6%) patients developed one alloantibody, 9 (9.5%) patients developed two alloantibodies and 2(2.1%) patients developed four alloantibodies. And 1(1.1%) developed five and six

alloantibodies. The most frequent combination was anti-E, anti-Kell combination which is detected in 5 patients.

These data are in accordance with those reported by (***Gader et al.,2008)*** who found a rate of alloantibody development is up to 22.06% in multi-transfused patients in Saudi Arabia and ***Ameen et al***., who found a rate of alloantibody development is up to 30% of Arab thalassemia major patients ***(Ameen et al., 2003)***.

Also ***(Sylvia et al., 2004 and Wangy et al., 2006)*** reported high results.

Other studies have reported a lower rate of alloimmunization that ranged from 2-20% in thalassemia patients of different ethnic origins (***Shamsian et al 2008; Bhatti., 2007; Noor Haslina., 2006; and Karimi., 2007).***

This high rate in our study may be due to the following:

* the majority of patients were transfused with blood matched for ABO&D antigens only, and the majority of red blood cell alloantibody formation was against the Kell and Rh blood group systems.

In contrast to some Western countries, it is not standard practice in Egypt to give phenotype-matched red cells to patients with thalassemia. The use of only phenotype-matched blood is controversial, especially in patients who have not yet

developed alloantibodies, as such blood is expensive and difficult to obtain. Therefore it has been suggested that phenotype matched blood be administered only to patients who have already been immunized and are at high risk of developing additional antibodies ***(Castro et al., 2002 and Wang et al., 2005).***

Previous reports have shown that reduction of red blood cell alloimmunization can be achieved by matching the blood for Rh and K antigens in transfusion-dependent thalassemia patients ***(Sylvia et al., 2004).***

* Also the majority of patients in our study had long term exposure to either non leucodepleted or post storage leucodepleted blood. Therefore the presence of residual donor white blood cells could have a potential influence on the rate of alloimmunization. This is in agreement with ***Ameen et al.*** results, who found a high rate of alloimmunization in patients who had long term exposure to either non leucodepleted or post storage leucodepleted blood ***(Ameen et al., 2003).***

In the present study the number of alloantibodies ranged from 1 to 6 with anti-E antibody being detected most frequently (13/52) representing 25%, the same as anti-Kell (13/52) representing 25% of alloantibodies found (table 13). This data is in accordance with that reported by ***Ameen et al. & Sylvia et al.,***

who found that anti-Kell and anti-E being the most frequent antibodies developing in their studied patients ***(Ameen et al., 2003; Sylvia et al., 2004).***

More recently (***Karimi .,2007, Noor Haslina .,2006 Wang et al.,2006***) reported nearly the same results they found that anti-Kell , anti-E and anti -D being the most frequent

However both ***Hok et al. and Pradhan et al.,*** who conducted their studies in Hong Kong & India respectively, reported that anti-Kell was not encountered in their studied thalassemia patients ***(Hok et al., 2001; Pradhan et al., 2001)***

This may be explained by the antigenic discrepancy between different populations with different ethnic and genetic backgrounds.

Formation of autoantibodies against RBCs has been documented in previous studies .Autoantibodies are directed against the individual's own RBCs which can result in clinical haemolysis and difficulty in cross-matching blood. Most autoantibodies react with high incidence antigens they agglutinate and sensitise the RBCs of random donors as well as those of antibody producers. This circulating humoral antibody may shorten the duration of RBC survival.

Patients with autoantibodies may have a higher transfusion rate and often require immunosuppressive drugs, splenectomy or alternative treatments***(Noor Haslina et al., 2007).***

In this study only one patient representing (1.1%) develoed autoantibodies that was in accordance with ***Noor Haslina*** Who find that Only one (1.6 percent) patient had autoantibodies without underlying alloantibodies, ***(Noor Haslina et al., 2007)*** the same results reported also by(***Bhatti et al., 2004***) and***(Karimi et al.,2007)***

However, a study in Kuwait observed that 11% of their patients developed autoantibodies with underlying alloantibodies. ***(Ameen et al., 2003).***

25 % autoantibodies also a high result has been founded by ***(Sylvia et al., 2004).***

The majority of patients in the present study had a long-term exposure to nonleukopoor and/or sub optimally leukoreduced blood. There was no statistically significant difference between patients who received non leucodepleted blood (20/64 patients developed alloantibodies; 31.2%) and patients who received post storage leucodepleted blood (7/31 patients developed alloantibodies ;(22.6 %) regarding the immunization rate *(P value >0.05)* (table 23).

The role of leukodepletion in preventing red cell alloimmunization has been described in several studies showing that patients receiving leukodepleted blood appeared to have a lower red cell alloimmunization rate, suggesting that it is the removal of leucocytes that reduces immune activation due to allogeneic transfusion ***(Shamsian et al., 2008, Sylvia et al., 2004.; Hok et al., 2001 and Blumberg et al., 2003).***

However, various studies have suggested that apoptosis and loss of viability of residual white cells in leukodepleted blood that have been stored before being transfused may lead to the release of immunostimulatory white cell antigens and soluble biologic mediators, resulting in sensitization of the recipients ***(Noor Haslina et al., 2007, Shamsian et al., 2008, Martelli et al., 2000 and Pistillo et al., 2001).***

This may explain why we continue to see alloimmunization in our patients even after we started using leukodepleted units as we only use the post storage leukodepletion which is a suboptimal method.

In our study there was no statistically significant difference between splenectomized (16/44 patients developed alloantibodies; 36.4%) and non splenectomized patients (11/51patients developed alloantibodies; 21.6%) *(P value*