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Probability of Finding an HLA-Matched Donor in Immediate and Extended Families: The Jordanian Experience

Wafa M. Elbjeirami [1], Fawzi Abdel-Rahman [2], Ayad Ahmed Hussein [2,*]

[1] Department of Cellular Therapy and Applied Genomics, King Hussein Cancer Center, Amman, Jordan
[2] Bone Marrow and Stem Cell Transplantation Program, King Hussein Cancer Center, Amman, Jordan

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A B S T R A C T

Information regarding the probability of finding HLA-matched related donor for a patient awaiting hematopoietic stem cell transplantation (HSCT) in developing countries is scanty. We performed a retrospective review of HLA genotypes and related data for 1254 consecutive patients and their families at King Hussein Cancer Center in Amman, Jordan, between 2003 and 2011 to evaluate the chance of finding HLA-matched donor. The median family size was 5 for all patients in the study (range, 1-14), and the average number of donors was 1.4 ± 0.9 for pediatric patients and 1.6 ± 0.9 for adults. Overall, the probability of finding an HLA-matched related donor at our center was 65.5% (60.6% in pediatric patients and 74% in adults). Of the total identified donors, 18% were nonsibling donors after an immediate and/or extended family search in the pediatric group, and 6% were nonsibling donors in the adult group. Overall, 13% of donors were nonsibling donors. We conclude that the probability of finding a matched related donor for HSCT in Jordan is much higher than that reported in Western countries and Asia (65% versus 25%). We expect a similar trend in other developing and Arab countries. We recommend integrating an extended family search before or concomitantly with an unrelated donor search.

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INTRODUCTION

Allogenic hematopoietic stem cell transplantation (HSCT) is the sole curative therapy available for many life-threatening malignant and nonmalignant disorders. Donor selection is a key component of the clinical practice of transplantation, with HLA-identical siblings the preferred donors [1]. In Western countries, approximately one-third of the patients in need of HSCT have HLA-identical siblings [2]. The common procedure in a search for an HLA-matched donor is to first examine the patient's siblings and parents. The best chance of finding a matched donor is within the nuclear family, followed by extended family.

The Middle Eastern region, including Arabic developing countries, consists of communities of large families with high population growth and density and many consanguineous marriages, which certainly increase the likelihood of finding a fully HLA-matched sibling donor. For example, the reported likelihood of finding a fully matched sibling donor is 60% in Saudi Arabia [3] and as high as 70% in some areas of Pakistan [4], much higher than the likelihood reported in European and North American patients [2]. In Jordan, the average number of children per family was once 5.6, but has dropped to 3.3 in the last fifteen years [5]. Recent data show a decline in consanguineous marriage among Jordanians from 63.7% [6] to 49%, in the last fifteen years with first-cousin marriages the most predominant type [7].

Limited data are available regarding the likelihood of having a matched related donor in developing and Arab countries. The aims of the present study were to evaluate the chance of finding a matched HLA-identical donor for Jordanian patients requiring HSCT and to determine the relevance of an extended family search in identifying matched related donors. We also report the prevalence of HLA phenotypes in the Jordanian population using a large pool of donors.

PATIENTS AND METHODS

Donor–Recipient Matching

A total of 1254 patients were consecutively tested at the Molecular Diagnostics and Immunogenetics Laboratory of King Hussein Cancer Center (KHCC) between January 2003 and December 2011. Characteristics of these 1254 patients are summarized in Table 1. The patient files were retrospectively screened for HLA class I and class II low-resolution typing of the patients and potential donors. Donors and recipients were antigen-matched (6/6) at the HLA-A, -B, and -DR loci through the HLA genotyping methodology described below. Demographic and clinical data were collected from the patients' medical files.

To better define the source of donors, we distinguished the matched sibling donors from nonsibling donors, with the latter including immediate family (ie, parents) and extended family (ie, any other related family member, eg, first cousins and blood-related uncles and aunts) who could be a potential donor. An extended family search was pursued in cases where the parents were close relatives (ie, consanguineous marriage); thus, blood-related uncles and aunts were considered likely donor candidates. Alternatively, in cases where 2 married individuals each from a patient's paternal or maternal side were identified, then HLA typing was performed in their offspring (ie, the patient's cousins).

HLA Genotyping

HLA typing was done with PCR–sequence-specific primers (PCR-SSPs) using a MicroSSP Generic HLA Class I and Class II ABDR DNA Typing Tray (One Lambda, Canoga Park, CA). In brief, DNA was extracted from peripheral blood collected in EDTA tubes using a Gentra Puregene Blood Kit (Qiagen, Crawley, UK) according to the manufacturer's instructions. DNA quantity was assessed with a NanoDrop 1000 spectrophotometer (Thermo Fisher Scientific, Waltham, MA), and purity was evaluated by calculating the 260/280 ratio. All DNA was stored at −20°C until testing. Data were interpreted using the worksheets provided by the manufacturer. HLA-A, -B, and -DR high-resolution typing was routinely applied when identity could not be ascertained by descent and when evaluating nonsibling donors. Donors with the best matching type and the highest resolution available were selected for confirmatory typing.

Allele Frequency Determination

Allele frequencies were calculated by dividing the total number of occurrences of that allele by the total number of alleles at that locus in the population, as described previously [8].

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* Correspondence and reprint requests: Ayad Ahmed Hussein, MD, King Hussein Cancer Center, Queen Rania Al Abdullah Street, PO Box 1269 Al-Jubeiha, Amman 11941, Jordan.
E-mail address: aahmed@khcc.jo (A.A. Hussein).

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Table 1
Descriptive Patient Data

	All Patients	Pediatric	Adult
Total number	1254	815 (65)	439 (35)
Age group, years, n (%)			
0-5		246 (30)	
6-12		364 (45)	
13-18		205 (25)	
18-35			262 (60)
36-50			131 (30)
>50 years			46 (10)
Sex, n (%)			
Male	735 (58.6)	469 (57.5)	266 (61)
Female	519 (41.4)	346 (42.5)	173 (39)
Disease, n (%)			
Malignant	685 (56)	320 (39)	385 (87.7)
Nonmalignant	535 (44)	495 (61)	54 (12.3)
Donor availability, n (%)			
Donor	821 (65.5)	494 (60.6)	327 (74)
No donor	433 (34.5)	321 (39.4)	112 (26)
Donor status, n (%)			
Sibling	715 (87)	407 (82)	308 (94)
Nonsibling related	106 (13)	87 (18)	19 (6)
Immediate family	85 (80)	72 (83)	13 (68)
Extended family	21 (20)	15 (17)	6 (32)

Statistical Analysis

All patient and donor data was entered into an Excel spreadsheet (Microsoft, Redmond, WA). Counts, percentages, and medians are provided for basic data description purposes. For some tables, data are summarized by mean ± SD for continuous variables and by number and percentage for categorical variables. The probability of finding a matched donor was determined by calculating the percentage of patients with at least one matched donor (6 of 6 antigens). Data analyses were done using SPSS 16.0 (SPSS, Inc., Chicago, IL).

RESULTS

Patient Characteristics

A total of 1254 consecutive patients examined at KHCC between 2003 and 2011 were analyzed retrospectively. Each screened patient was assigned to the adult (age >18 years) or pediatric group, and each group was further subdivided into age groups. Characteristics of the 1254 patients included in the study are presented in Table 1. The majority of patients (65%) were age <18 years, with the largest disease-conflicted group clustered at age 6-12 years (45%). Similarly, a significantly high percentage of adult patients (60%) were clustered in the 18-35 year group. Males were predominant over females in both the pediatric and adult groups (57.5% versus 42.5% and 61% versus 39%, respectively). Overall, for all patients, the probability of having an HLA-matched donor was 65%, with a higher value in adults (74%) compared with the pediatric group (60.6%).

Probability of Finding a Matched Donor

We first analyzed the family size of overall patients to identify any correlation with donor availability. We found no significant differences in median family size between patients with at least 1 matched donor and those without a matched donor (Table 2). In other words, donor availability was not correlated with immediate family size.

We divided the adult and pediatric groups into 3 age subgroups each. We analyzed donor availability for each age group and compared the overall respective pediatric and adult results. In the pediatric group, there was a trend toward an increasing percentage of patients with an HLA-matched donor with increasing patient age (Table 3). The adult group overall exhibited a similar trend of donor availability, but subgroup 6 patients (age >50 years) had a significantly lower percentage of patients with an HLA-matched donor (67%) compared with subgroups 4 and 5 and the overall adult availability of 74% (Table 4). In the pediatric group, the average number of available donors was almost identical in subgroups 1, 2, and 3 (1.35, 1.4, and 1.4 donors per patient, respectively) (Table 3). In contrast, adult patients had an average of 1.6 matched donors for subgroup 4, 1.8 for subgroup 5, and 1.5 for subgroup 6 (Table 4). The slightly higher average numbers of HLA-matched donors in the adults in contrast to the pediatric group is reflected in the higher percentage of donor availability for adult patients overall (74%) compared with the pediatric group overall (60.6%).

Table 2
Patient Family Size and Donor Data in All Subgroups

	Value
Family size, median (range)	
All patients	5 (1-14)
Patients with donors	5 (1-13)
Patients with sibling donors	5 (1-13)
Patients with nonsibling donors	4 (1-13)
Patients without donors	4 (1-14)
Donor availability, median (range)	
All patients	1 (1-7)
Patients with sibling donors	1 (1-6)
Patients with nonsibling donors	1 (1-4)
Patients with extended family donors	1 (1-7)

Donor source was categorized as HLA-matched sibling, nonsibling (including parents and all related family members), or extended-family donor (including blood-related non–immediate family members only). Interestingly, 18% of overall HLA-matched donors were nonsibling blood relatives, with 17% of them non–immediate family members (Table 3). In contrast, only 6% of all HLA-matched donors were nonsibling related in the adult group (Table 4). The distribution of HLA-identical sibling donors versus related immediate or extended family donors did not differ among the pediatric and adult subgroups.

HLA Phenotype and Haplotype Frequencies in the Jordanian Population

The frequencies of HLA-A, -B, and -DR are presented in Table 5. A total of 20 HLA-A antigens, 30 HLA-B antigens, and 20 HLA-DR antigens were detected. The most frequent HLA-A locus was HLA-A*02 (21.3%), followed by HLA-A*01 (15%) and then HLA-A*24 (10.4%). The antigens detected at the highest frequencies for the HLA-B locus were HLA-B*35 (14%), HLA-B*51 (9.9%), HLA-B*49 (6.7%), and HLA-B*50 (6.6%). Data analysis identified the 3 most prevalent DRB1* phenotypes in the study group as DRB1*11, DRB1*04, and DRB1*13, with respective frequencies of 20.6%, 16.2%, and 14.4%. The most frequent haplotypes seen in the Jordanian population are listed in Table 6: HLA-A*02-B*50-DR*07 (0.039), HLA-A*02-B*51-DR*04 (0.028), and HLA-A*24-B*35-DR*11 (0.023).

Table 7 compares gene frequencies for HLA-A, -B, and -DR among different ethnic populations. As expected, the gene frequency pattern of the Jordanian population is more closely related to the patterns reported in Saudi Arabians [9], Turks [10], and some Caucasians [8,11] than to the patterns of Indians [12,13] and Asians [8,11]; however, Jordanians have higher gene frequencies of A*01, A*30, B*35, and B*49.

Table 3
Probability of Finding a Matched Donor in Pediatric Patients by Age Group

Donor Availability	Entire Age Group			0-5 Years (Group 1)			6-12 Years (Group 2)			13-18 Years (Group 3)		
	n (%)	Mean ± SD	Range	n (%)	Mean ± SD	Range	n (%)	Mean ± SD	Range	n (%)	Mean ± SD	Range
Patients without donors	321 (39.4)			105 (43)			149 (41)			67 (33)		
Patients with donors	494 (60.6)	1.4 ± 0.9	1-7	141 (57)	1.35 ± 1	1-7	215 (59)	1.4 ± 0.7	1-5	138 (67)	1.4 ± 0.6	1-6
Patients with sibling donors	407 (82)	1.45 ± 0.7	1-6	115 (82)	1.32 ± 0.6	1-3	180 (84)	1.4 ± 0.8	1-5	112 (81)	1.4 ± 0.6	1-6
Patients with non-sibling donors	87 (18)	1.5 ± 0.5	1-4	26 (18)	1.37 ± 1.2	1-7	35 (16)	1.4 ± 0.6	1-3	26 (19)	1.6 ± 0.8	1-3
Patients with extended family donors	15 (17)	2 ± 1.6	1-7	4 (15)	2.5 ± 3	1-7	9 (25)	1.8 ± 0.8	1-3	4 (15)	2 ± 1	1-3

DISCUSSION

Jordan has a population of approximately 5.6 million. The high rate of consanguineous marriage and environmental factors contribute to a high rate of genetic malignant and nonmalignant diseases that can be treated by HSCT, for which donors are required. Bone marrow and stem cell transplantation has been performed in Jordan since the early 1990s, but the first comprehensive program was not established until March 2003, at KHCC [14].

This is the first study to address the probability of finding HLA-matched related donors for Jordanian patients awaiting HSCT at KHCC. Overall, 65.5% of our patients had an identical HLA-matched blood-related donor (60.6% in the pediatric group and 74% in adults). Of the 377 patients who underwent matched related allo-HSCT at KHCC between January 2003 and the end of December 2011, 349 (92.5%) had a matched sibling donor (190 [77%] in the pediatric group) and 28 (7.5%) had a nonsibling family donor (26 [93%] in the pediatric group).

The high probability of finding a matched related donor in the Jordanian pool donor is higher than what has been reported in international searches for matched unrelated donors (MUDs), especially for Caucasian populations. Approximately 15 million international HSCT donors are currently registered in a network of interconnected hubs (National Hematopoietic Stem Cell Donor Registries [7,15]. In 2008, only 50%-60% of patients of Caucasian descent had a fully HLA-matched and available unrelated adult donor, and non-Caucasians had a substantially lower probability [16]. Indeed, according to data from the National Marrow Donor Program, only roughly 20% of Asians and 17% of African Americans will find a fully HLA-matched and available unrelated adult donor [16]; however, in Austria, the likelihood of identifying a suitable MUD for patients is reportedly 68.9% [7]. This high success rate in the donor search for patients of Austrian descent is likely attributed to the small Austrian ethnic population pool, which increases the chance of finding an MUD. Similarly, Heemskerk et al. [17] reported that over the last 10 years, an unrelated donor could be found for 84% of HSCT recipients in a mainly Dutch patient population. The Jordanian population comprises 98% Arabs, 1% Circassians, and 1% Armenians, and overall can be considered to represent a single major ethnic group in which a potential MUD exists for the patients with no donor. It is possible that patients of ethnic minority have a smaller pool of registered marrow donors in international registries. Indeed, the chance of finding a matched HSCT donor for a Jordanian patient from the international unrelated stem cell registries is only 2%-5%. Other potential factors that may contribute to the low matched donor availability are the decline in consanguineous marriages (~23%) and decrease in family size (~41%) seen in Jordan over the last decade [7]. As would be expected, increasing family size increases the likelihood of identifying an HLA-matched donor. This is reflected in our patient data, with a greater chance of finding a donor seen in the older age subgroups. However, the decline in consanguineous marriage rate and family size could have a constrictive effect on the likelihood of identifying a matched related donor, by diminishing the necessary combinations of HLA determinants found in the patients. This can be rectified by establishing a national donor registry in Jordan, to increase the chance of identifying a MUD for patients with no donor and patients of ethnic minorities or mixed ancestries.

In a Saudi study, Jawdat et al. [3] examined different variables for possible associations with the increased likelihood of finding an HLA-matched sibling donor in older patients. Similar to their results, our findings showed no correlation with sex (data not shown). However, based on the observed increased likelihood of finding a matched donor in adult and pediatric groups, our findings support that older patient age is associated with an increasing number of siblings to screen. Indeed, the likelihood of finding a matched donor was greater in patients age 18-35 years

Table 4
Probability of Finding a Matched Donor in Adult Patients by Age Group

Donor Availability	Entire Age Group			18-35 Years (Group 4)			36-50 Years (Group 5)			>50 Years (Group 6)		
	n (%)	Mean ± SD	Range	n (%)	Mean ± SD	Range	n (%)	Mean ± SD	Range	n (%)	Mean ± SD	Range
Patients without donors	112 (26)			65 (25)			32 (24)			15 (33)		
Patients with donors	327 (74)	1.6 ± 0.9	1-5	197 (75)	1.6 ± 0.6	1-5	99 (76)	1.8 ± 0.6	1-5	31 (67)	1.5 ± 0.6	1-3
Patients with sibling donor	308 (94)	1.7 ± 0.6	1-5	186 (94)	1.6 ± 0.9	1-5	93 (94)	1.8 ± 0.8	1-5	29 (94)	1.5 ± 0.6	1-3
Patients with non-sibling donor	19 (6)	1.4 ± 0.5	1-2	11 (6)	1.6 ± 0.6	1-3	6 (6)	1.5 ± 0.5	1-2	2 (6)	1 ± 0	1
Patients with extended family donor	6 (32)	1.3 ± 0.5	1-2	3 (27)	1.3 ± 0.5	1-2	2 (33)	1.5 ± 0.7	1-2	1 (50)	—	—

Table 5
Frequency of HLA-A, -B and DR Antigens in the Jordanian Population

HLA-A	Number	Frequency, %	HLA-B	Number	Frequency, %	HLA-DR	Number	Frequency, %
01	354	14.7	07	67	2.7	01	109	4.8
02	532	22.0	08	57	2.3	03	276	12.1
03	219	9.1	13	71	2.9	04	382	16.7
11	103	4.3	14	107	4.4	07	242	10.6
23	96	4.0	15	114	4.7	08	52	2.3
24	259	10.7	18	130	5.3	09	8	0.3
25	4	0.2	27	40	1.6	10	63	2.8
26	126	5.2	35	365	14.9	11	482	21.1
29	62	2.6	37	17	0.7	12	23	1.0
30	219	9.1	38	114	4.7	13	332	14.5
31	55	2.3	39	39	1.6	14	86	3.8
32	73	3.0	40	54	2.2	15	211	9.2
33	81	3.4	41	142	5.8	16	20	0.9
34	19	0.8	42	22	0.9			
36	4	0.2	44	137	5.6			
43	0	0.0	45	40	1.6			
66	20	0.8	46	1	0.0			
68	121	5.0	47	12	0.5			
69	46	1.9	48	0	0.0			
74	19	0.8	49	153	6.2			
80	3	0.1	50	157	6.4			
			51	252	10.3			
			52	119	4.9			
			53	50	2.0			
			54	1	0.0			
			55	31	1.3			
			56	6	0.2			
			57	78	3.2			
			58	57	2.3			
			59	0	0.0			
			67	0	0.0			
			73	15	0.6			
			78	0	0.0			
			81	0	0.0			
			82	1	0.0			
			83	0	0.0			

than in those age 0-5 years (~75% versus 57%). Thus, the likelihood of finding a matched donor is greater in the older patients in both the pediatric and adult groups.

Previous studies have shown equivalent survival in patients with hematologic malignancies who underwent HSCT with a graft from a related donor who was phenotypically HLA-matched and those who did so with a graft from a genotypically HLA-matched sibling [18]. In our institution, for patients lacking an HLA-identical sibling donor or other immediate family donor (ie, parent), an extended family search is pursued simultaneously with a search for an unrelated donor. Jawdat et al. [3] reported no correlation between consanguineous marriage and finding a matched sibling donor; however, at our center, 13% of potential HLA-matched donors are from the immediate or extended family, with the highest number in the 13- to 18-year age group. To our knowledge, the literature contains no data regarding the actual likelihood of finding an HLA-matched donor in the patient's immediate or extended family.

Table 6
Haplotype Frequencies in the Jordanian Population

Haplotype	Frequency
HLA-A*02 B*50 DR*07	0.0386
HLA-A*02 B*51 DR*04	0.0276
HLA-A*24 B*35 DR*11	0.0234
HLA-A*24 B*18 DR*11	0.0193
HLA-A*01 B*35 DR*11	0.0166
HLA-A*24 B*35 DR*04	0.0152
HLA-A*02 B*41 DR*04	0.0138
HLA-A*03 B*51 DR*11	0.0138
HLA-A*33 B*14 DR*04	0.0138
HLA-A*30 B*49 DR*13	0.0124
HLA-A*30 B*53 DR*13	0.0124
HLA-A*29 B*18 DR*04	0.0124
HLA-A*02 B*35 DR*11	0.0124
HLA-A*03 B*51 DR*07	0.0124
HLA-A*01 B*52 DR*04	0.0110
HLA-A*11 B*35 DR*04	0.0110
HLA-A*02 B*51 DR*11	0.0110
HLA-A*11 B*52 DR*15	0.0110
HLA-A*24 B*15 DR*13	0.0110

Schipper et al. [19] developed a procedure for calculating the probability of finding a suitable donor among a patient's extended family. This procedure relies on a large extended family, which applies to the Jordanian population, and on the frequencies of haplotypes involved. At our center, we strive to deduce the family tree of patients to pinpoint potential extended family donors, as evidenced by the significant number of blood-related donors identified. Another pertinent consideration is that our results are based on the number of donors tested at our center, which might not reflect the true number of blood-related donors, suggesting an even higher likelihood of finding extended family donors.

Comparing our reported HLA class I and II profiles with those reported from Saudi Arabia [9], Turkey [10], India [12,13], Caucasian populations [8,11], and Asians reveals that the Jordanian pool is generally more closely related to the Saudi and Turkish populations. Overall, these observations are consistent with recognized historical, geographical, cultural, ethnic, and linguistic relationships among these

Table 7
Comparison of Main Gene Frequencies of HLA Phenotypes in Jordan and Other Ethnic Populations

HLA	Jordan	Saudi Arabia	Turkey	India	Caucasian	Asian
HLA-A	(n = 2415)	(n = 383)	(n = 228)	(n = 91)	(n = 265)	(n = 358)
02	22.0	30.4	21.9	9.6	27.1	9.5
01	14.7	6.8	6.6	12.3	15.1	1.5
24	10.7	6.7	21.3	16.7	6.6	18.9
03	9.1	6.3	10.9	9.3	12.6	1.0
30	9.1	5.2	1.3	1.1	1.1	1.8
HLA-B	(n = 2449)	(n = 383)	(n = 228)	(n = 91)	(n = 265)	(n = 358)
35	14.9	8.2	14	5.6	6.8	3.9
51	10.3	12.8	15.8	6.8	5.7	6.7
50	6.4	3.3	6.6	0.7	0.6	0
49	6.2	18.8	5	3.6	0.9	0.1
41	5.8	3.5	13.4	10.5	11.7	4.4
HLA-DR	(n = 2286)	(n = 383)	(n = 228)	(n = 102)	(n = 232)	(n = 232)
11	21.1	7.8	35.4	17.7	9.7	8.3
04	16.7	18.9	13.1	8.8	12.8	14.4
13	14.5	13.8	6.2	15.2	12.7	3.0
03	12.1	15.4	9.6	10.3	10.1	2.9
07	10.6	17.8	11.7	8.8	15.1	16.3

populations and suggest that Jordanian HSCT recipients have a greater likelihood of finding a phenotypically matched donor in registries based on these populations. Furthermore, to date only 1 study has examined HLA profiles in the Jordanian population: a survey by Sánchez-Velasco et al. [20] of a small pool of 100 adults from Amman and 46 adults from the Jordan River valley. In the present study, we examined a significantly larger pool of Jordanians from various regions of the country. In contrast to our data, Sánchez-Velasco et al. [20] reported the most frequent HLA-A loci as HLA-A*02 (13.4%), HLA-A*30 (9.3%), HLA-A*01 (7.9%), HLA-A*11 (7.9%), and HLA-A*24 (5.9%). Although 4 of these phenotypes were also among the top 5 most observed in our data, A*11 (4.3%) was not identified as such. For HLA-B, Sánchez-Velasco et al. [20] identified B*07 as the most frequent locus (17.2%), followed by B*35 (8.3%), B*51 (6.6%), B*08 (3.8%), and B*44 (2.8%). We identified B*35 as the most frequent locus in our Jordanian population, but found no significant frequency of B*07 or B*08. Finally, Sánchez-Velasco et al. identified the most frequent DRB1 allele in their Jordanian population as DRB1*07 (25.5%), followed by DRB1*04 (19.7%), and DRB1*15 (8.9%). In our much larger population pool, DRB1*11 was the most frequently detected locus; DRB1*15 frequency was 9.2%, comparable to that reported by Sánchez-Velasco et al. Overall, the high prevalence of gene frequencies reported by our group and by Sánchez-Velasco et al. [20] can be explained by the continued high frequency of consanguineous marriages in Jordan.

The most common HLA-A-B-DRB haplotype in our Jordanian population was HLA-A*02-B*50-DR*07 (3.9%), which is also very common in Tunis (3%) and United Arab Emirates (4.8%) [21]. This haplotype also has been reported in Mongolians (3.2%), Manchu (2.2%), Spaniards (1.2%), and Italians (0.5%) [21]. The HLA-A*02-B*51-DR*04 haplotype was identified in 2.8% of our study population, compared with 7.2% of the Pakistani population but <0.1% of Caucasians in western Europe [22]. The 2.3% frequency of HLA-A*24-B*35-DR*11 in our population is comparable to that reported in Austrians (2.7%), Germans (1.4%), and Italians (1.4%) [21], but significantly lower than that reported in Georgians (5.7%) [23]. Finally, the HLA-A*24 B*18 DR*11 haplotype was identified in 1.9% of our population, compared with 2.1% of Armenians and 0.7% of Italians [21]. The low occurrence of the most common Jordanian haplotypes in other populations reiterates again the critical need for a local donor registry. The probability of finding an MUD in national and international registries is dependent on the frequency of haplotypes among different populations. This is evident from the patient and donor lists in our center, in which patients without a matching related donor have an only 1 in 50 chance of finding a MUD in European donor registries. Taking into consideration the geographical and cultural similarities between Jordan and its neighboring Arabic countries, a higher likelihood of finding a MUD in established donor registries of Arabic origin will be a better alternative for both Jordan and its neighbors.

In conclusion, our Jordanian patients' chance of finding an HLA-matched donor appears to be high because of the increased probability of finding an identical donor in the immediate and extended families. A future study will compare clinical outcomes in recipients of HSCT with a related donor and those with a genotypically HLA-matched sibling. Our conclusions are strengthened by the fact that this is a population-based, single-center study with a relatively large number of patients and donors. Our data confirm the feasibility of using HLA-related donors to avoid lengthy matching procedures and provide patients with identical haplotypes instead of mere matching at the phenotypic level. Furthermore, HLA typing of extended family donors along with immediate family and sibling donors can provide the transplant physician with more flexibility in final donor selection and identification of a readily available backup matched donor. Thus, we recommend integrating donor search process in the extended family concomitant with an unrelated donor search. This recommendation also can be applied to Western subpopulations whose origin descends from ethnic groups with a similar pattern as the Jordanian population.

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