

Challenges faced by Bone Marrow Registries in India

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1. INTRODUCTION

Hematopoietic stem cell transplantation (HSCT) is the transplantation of multipotent hematopoietic stem cells, usually derived from bone marrow, peripheral blood, or umbilical cord blood. It is a medical procedure in the fields of hematology, most often performed for patients with certain cancers of the blood or bone marrow, such as multiple myeloma¹ or leukemia².

The success of HSCT depends on finding cell donors who are closely matched genetically; as the degree of mismatching increases, the success of unrelated donor HSCT falls accordingly³. A patient's ideal donor is a genetically matched sibling. Using unrelated adult donors to facilitate HSCT has provided a major opportunity for patients without a matched sibling donor. This was the driving force that encouraged development of Marrow donor registries in world. The first registry was established in UK for a patient called Anthony Nolan who required an unrelated donor way back in 1974.

In India many attempts to establish a marrow donor registry have been made by various groups. DATRI Blood Stem Cell Donors Registry and Marrow Donor Registry India (MDRI) are currently the two major registries working in India. As of April 2014, *Datri* has successfully facilitated 52 Blood Stem Cell transplants and have a database of more than 56,000 registered *donors*.

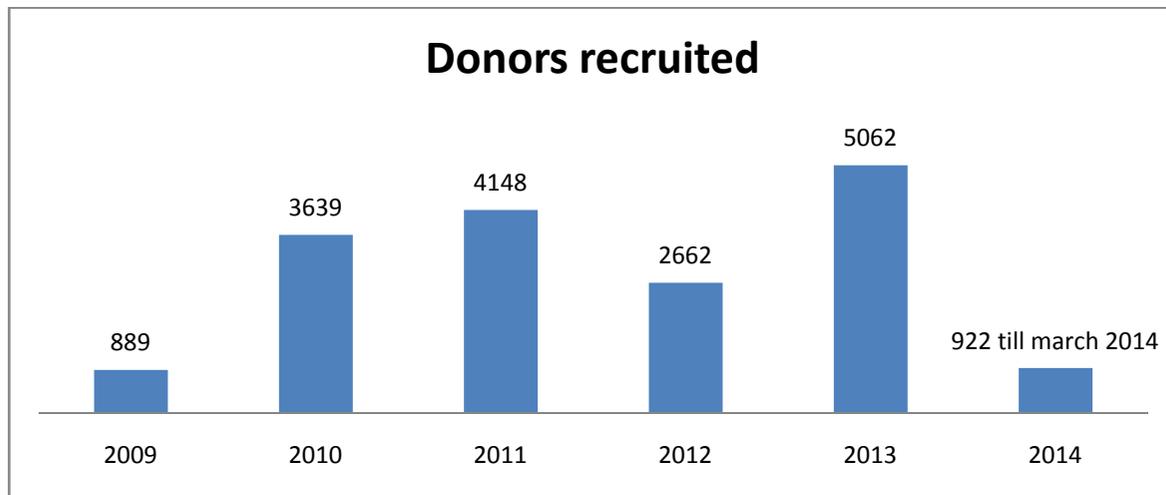
Marrow donor registry India (MDRI) was established in 2009 with the aim of helping patients searching for an unrelated donor to undergo stem cell transplantation. From 2009 to till date MDRI has about 17800 voluntary donors that have pledged their stem cells.

Here we would like to share the challenges faced by MDRI in past 5 years after its establishment.

1. **Lac of awareness:** People are unaware of the terms such as stem cell donations and hence are reluctant to come forward and register with us. MDRI conducts awareness programs

and counseling sessions for all those who wish to register as donors. The aim of these awareness programs is to break the myths and clarify doubts in the minds of potential donors in order to help them make informed decision regarding becoming a donor. We have achieved the number of 17800 donors after 5 years of establishment of MDRI.(see table1)

Table 1: Annual Donors recruitment in MDRI



2. **Lac of funds for treatment:** Patients in India come from poor to middle class families and most of the times are unable to complete treatment and hence undergoing a bone marrow transplant is a great financial challenge to the patient and their families. The cost of HSCT in USA would cost an Indian patient about 150000 US\$ whereas HSCT in India would cost about 30000 US\$. When Indian donors are available for transplant and additional 20000 US\$ are saved per transplant which are used as fees to search and procure matched stem cells from abroad.

3. **Lac of matched donors:** As it is a known fact worldwide that only 25-30% patients will find a matching donor from his/her family. The remaining donors will have to look for an unrelated donor outside their family. India is the second most populated country in the world with population of 1.27 billion and has been subjected to different waves of immigration. With 22 official languages, India has amalgamation of various ethnicities, cultures, languages, marriages within communities which have resulted in unique gene pool. (see fig 1)

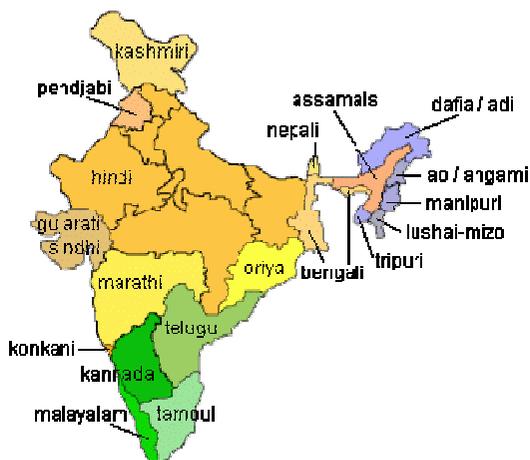


Fig 1: Map of India describing most common languages spoken

HLA genes are most polymorphic in human genome. HLA genes play a central role in immunity and are responsible for graft rejection in hematopoietic stem cell transplantation. As the HLA loci depict an immense degree of polymorphism and extensive tight-linkage among loci, it helps to determine genetic relatedness amongst population and population migration pattern etc. The distribution of MDRI donors based on the languages spoken is given in Fig 2.

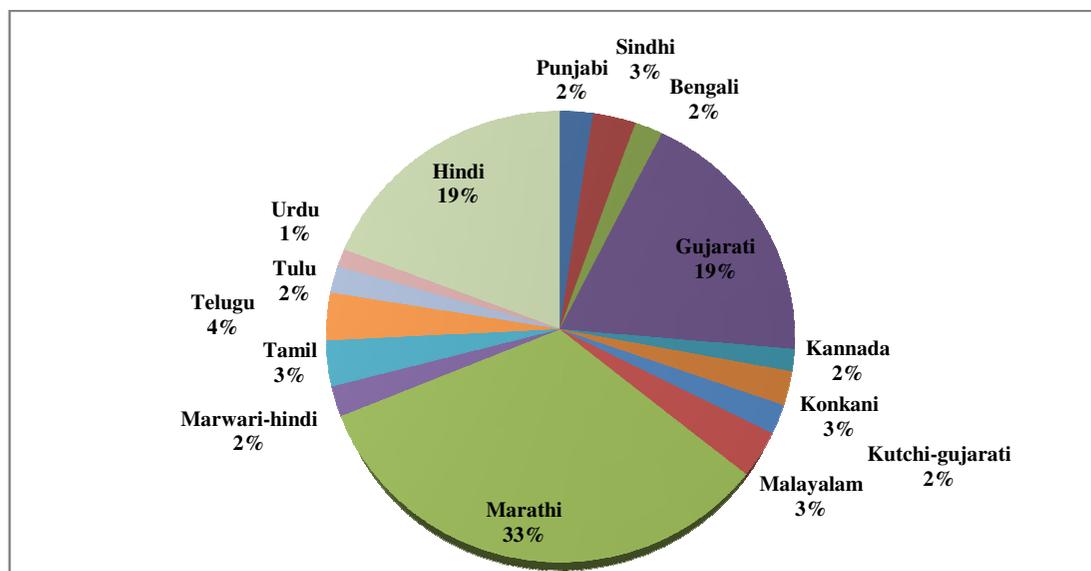


Fig 2. Distribution of MDRI donors in 16 linguistic groups.

Indian haplotypes show some unity in diversity in their HLA gene inheritance. Although many common haplotypes are seen across all linguistic groups some unique HLA haplotypes distinguish one group from another. Being a registry this knowledge will help us understand the HLA genetics of Indian population and help us find suitable matched donors for the patients in need for transplant. Tables 2 and 3 show the common and unique haplotypes in MDRI donors.

Table 2: Most common HLA haplotypes in MDRI donors

A	B	DR	RANK in 16 groups	HAP-FREQUENCY %
A*33	B*44	DRB1*07	Rank one in 7 groups	3.041%
A*01	B*57	DRB1*07	Rank one in 3 groups	2.395%
A*02	B*40	DRB1*15	Rank one in Urdu group	1.797%
A*24	B*40	DRB1*15	common across all groups	1.2%

Table 3: Unique haplotypes in MDRI donors

A	B	DR	HAP-FREQ%	RANK	GROUP
A*02	B*15	DRB1*15	2.6%	4	Bengali
A*24	B*15	DRB1*15	3.0%	2	Bengali
A*02	B*40	DRB1*14	2.4%	4	Kutchi
A*11	B*35	DRB1*13	2.0%	5	Kutchi
A*11	B*52	DRB1*14	3.3%	2	Kutchi
A*26	B*08	DRB1*03	2.5%	3	Kutchi
A*11	B*35	DRB1*11	3.4%	2	Konkani
A*02	B*07	DRB1*15	3.4%	3	Konkani
A*11	B*07	DRB1*15	2.1%	4	Kannada
A*24	B*40	DRB1*14	2.3%	4	Malayalam
A*33	B*58	DRB1*13	2.5%	3	Malayalam
A*29	B*07	DRB1*10	2.42%	3	Marathi

A*11	B*52	DRB1*15	2.3%	5	Marathi
A*24	B*07	DRB1*15	2.5%	2	Tamil
A*02	B*35	DRB1*15	2.1%	4	Telegu
A*11	B*35	DRB1*15	2.6%	2	Urdu
A*33	B*58	DRB1*03	3.8%	4	Sindhi
A*24	B*18	DRB1*11	4.6%	2	Sindhi
A*02	B*50	DRB1*03	2.3%	6	Sindhi
A*33	B*14	DRB1*01	11.5%	1	Parsi
A*02	B*73	DRB1*04	7.7%	3	Parsi

All these variations suggest the inbuilt customs and traditional practices of marriage system generate unique pools of genes in spite of the same geographical region. Unique haplotype patterns in each group reveals that more donor drives have to be concentrated on those groups that are poorly represented in the donor pool. This will increase the chances of finding the match within the same linguistic group.

5. Lac of funds for function of registry: As marrow donor registries in India are not supported by the state or central government of India. Each functioning registry is dependent on funding from various private organizations. Few patients and their families who understand the problems faced by registries help in fund raising. Each step in the functioning of the registry from organizing donor camps, testing of donors for HLA typing, maintenance of the laboratory and wages of staff requires a large financial backup which is very difficult to achieve.
6. Donor dropout rates: Control of the donor dropout rates at important stages before transplant remains a major challenge faced by all registries world-wide. At MDRI we initiated donor searches in 2012 when our registry reached donor strength of 10000 donors.

Stages of donor dropout at MDRI

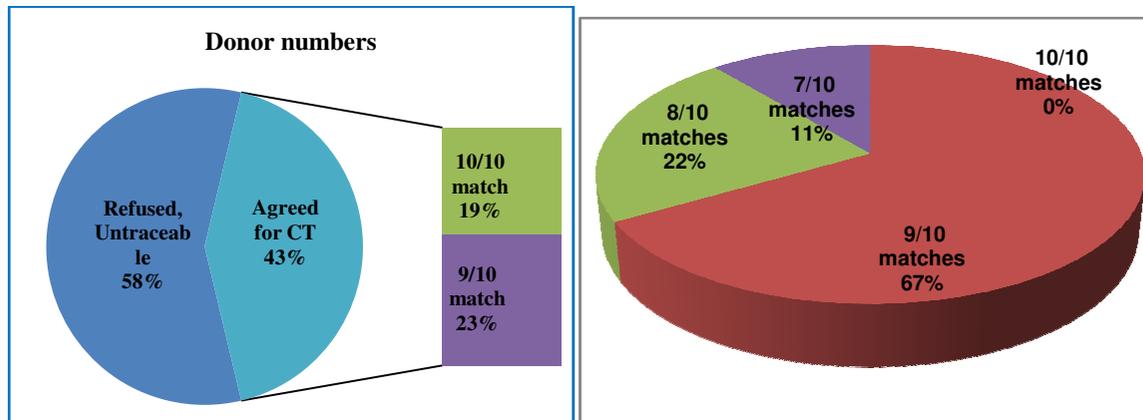
- At MDRI, a donor that matches a patient at 6/6 low resolution level is contacted for further confirmatory testing for all 10 alleles

- When the donor matches at 10/10 low resolution he is again contacted for consent for high resolution typing followed by stem cell donation. So far no donor has matched at 10/10 high resolution level to facilitate a transplant from MDRI.

The statistics of donor dropout rates at both these steps are shown in figure 3 and 4

Figure 3: donor dropout rate at low resolution matching level

Figure 4: high resolution level donor matching rates.



REFERENCES

- [1] Bladé J, Samson D, Reece D, et al. (1998). "Criteria for evaluating disease response and progression in patients with multiple myeloma treated by high-dose therapy and haemopoietic stem cell transplantation. Myeloma Subcommittee of the EBMT. European Group for Blood and Marrow Transplant". *Br. J. Haematol.* 102 (5): 1115–23.
- [2] Pavletic SZ, Khouri IF, Haagenson M, et al. (2005). "Unrelated donor marrow transplantation for B-cell chronic lymphocytic leukemia after using myeloablative conditioning: results from the Center for International Blood and Marrow Transplant research". *J. Clin. Oncol.* 23 (24): 5788–94.
- [3] J Pidala, J Kim, M Schell, S J Lee, R Hillgruber, et al. Race/ethnicity affects the probability of finding an HLA-A, -B, -C and -DRB1 allele-matched unrelated donor and likelihood of subsequent transplant utilization *Bone Marrow Transplantation* (2013) 48, 346–350.