

Human Leukocyte Antigen-Matched Unrelated Donor Search Experience for Hematological Disorder Patients Requiring Transplant: Scenario for Indian Patients

Abstract

Introduction: Human leukocyte antigen (HLA)-matched unrelated donor (MUD) is the source of MUD transplantation (MUDT) for about 70% of patients who do not have matched related donor. To facilitate MUD search globally, there are 75 stem cell registries with more than 28 million donors registered (as of January 2017). Out of these donors, India has an insignificant representation of approximately 0.23 million. Further, Indians express high genetic variations, making it difficult to find MUD for an Indian patient. **Aims and Objectives:** The aim of this study is to analyze the MUD search for hematological disorder patients requiring transplant. An attempt was made to observe the MUD scenario for Indian patients requiring MUDT from accessible stem cell registries. **Methods:** A total of 558 patients approached Genebandhu registry and Chimera Transplant Research Foundation for MUD search over a period of 4 years requiring MUDT were included in this study. High resolution of HLA-A, -B, -C, -DRB1, and -DQB1 was used to perform MUD search through proprietary software called Prometheus and Bone Marrow Donors Worldwide (BMDW) search tool. **Results:** Out of 558 patients, MUD was located only for 135 (24.19%) patients. Out of these 135 patients, 91 (16.30%) patients found an MUD in global database and only 44 (7.88%) patients within India. **Conclusion:** This study demonstrates that building a large Indian database will not only help in increasing the chances of finding an MUD for maximum number of patients within India but also provide cost-effective treatment, in a society where cost is a vital factor.

Keywords: Hematological disorders, human leukocyte antigen, matched unrelated donor, matched unrelated donor transplantation

Introduction

Every 6 min, somebody in India is diagnosed with hematological disorders.^[1] Hematopoietic stem cell transplantation (HSCT) is typically the favored curative treatment for patients with such disorders,^[2] but its use has been reduced as a result of inadequate donor availability in the form of either matched related donor (MRD) or matched unrelated donor (MUD). Only about 30% of the patients have suitable MRD as a source for stem cell transplant. Hence, MUD has to be the source of HSCT for approximately 70% of patients.^[3] In India, HSCT has developed rapidly as a care of treatment, with increase in the number of hospitals undertaking this treatment. However, volunteer stem cell registry development in India has lagged behind.^[4] The study was performed at Genebandhu registry^[5] and Chimera Transplant Research Foundation

currently working in the area of MUD transplantation (MUDT).

Methods

Study type

This was an observational study where HLA data of 558 patients were used to carry out an MUD search to see the MUD Scenario for Indian patients requiring MUDT from all accessible stem cell registries. Informed consent was obtained from participating human subjects.

Search tool used for matched unrelated donor search

Prometheus

It is an informatics tool for stem cell donor registries by Steiner Ltd. It covers all the major processes of the registry's routine work including international donor search process.^[6]

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Bone Marrow Donors Worldwide

A web portal which contains the data of marrow donors which includes centralized data on HLA phenotypes imported from various registries across the world and can be accessed globally.^[7]

Patient human leukocyte antigen reports

The (558) patients who approached Genebandhu registry through their transplant center were included in this observational study. All these patients were high-resolution HLA-A, -B, -C, DRB1, and DQB1 loci typed.

Matched unrelated donor search process

The MUD searches for these patients (558) were made using aforesaid search tool. To initiate a search in addition to HLA report, demographic information including (age, gender, and clinical diagnosis) were registered in both the search tools.

Designing a matched unrelated donor search strategy

The search result was considered a “match” when 10/10 potential match was found in Indian and global donor database.

Results

A total of 558 patients requiring MUDT approached Genebandhu registry and Chimera Transplant Research Foundation for MUD search from May 2012 to August 2016 were included in the study. Out of 558 patients requiring MUD, 401 were male and 157 were female. Search result for MUD and patients who found 10/10 MUD was prepared month wise and is shown in Figure 1.

We were able to locate an MUD for 135 (24.19%) patients. Out of these 135 patients, 91 (16.30%) found an MUD in the global database while only 44 (7.88%) patients could find it within India [Figure 2].

Discussion

In the present MUD search experience for Indian hematological disorder patients requiring MUDT from

all accessible stem cell registries, we have seen that the chances of finding MUD for Indian patients either in global or Indian donor data pool are not significant. As reported earlier, the probability of finding an allele match for an Indian patient in the multinational HLA registries is 16% and a dismal 0.008% in the Indian registries due to the fact that donors in Indian registries are just 33,678 as compared to 22.5 million in Bone Marrow Donors Worldwide (BMDW).^[2] Currently, donors in Indian registries are approximately 0.23 million as compared to 28.5 million in BMDW.^[7] This indicates that the increasing number of registered donors from 33,678 to 0.23 million in Indian donor data pool has clearly enhanced the chances of finding an MUD within India. As per our MUD search experience, 7.88% of patients [Figure 2] were lucky enough to find an MUD within Indian donor data pool. Whereas the number of donors in BMDW increases from 22.5 million to 28.5 million, but there has been no significant increase in the chances of finding an MUD within global database for Indian patients. It implies that the size and genetic composition of the data in such registries determine the chances of finding MUD for an Indian patient who does not have an MRD. These data also demonstrate that the chances of finding a match would proportionately increase when the number of donors increases in Indian database, although the increase in non-Indian donors does not appear to have much impact. Further, it can also be explained by the uniqueness of Indian genetic pool, while the global database is predominantly composed of Caucasian population. Key planning and strategy for donor recruitment are urgently needed for recruiting more number of donors which will ultimately result in better likelihood of finding a MUD. The major challenges faced by the bone marrow registries are lack of awareness, patient's economic status, unavailability of unrelated-matched donors, lack of funding for the function of registry, and high donor dropout rates.^[8] As per the ICMR incidence data generated by population-based cancer registries in India, there is a continuous rise in the detection of leukemia patients across the globe, with around 104,239 cases being reported in

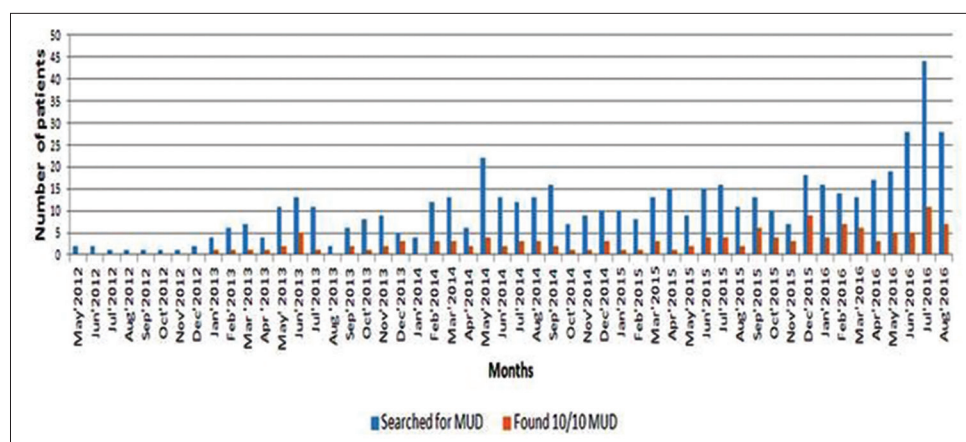


Figure 1: Month-wise search result for matched unrelated donor and patients who found 10/10 matched unrelated donor from May 2012 to August 2016

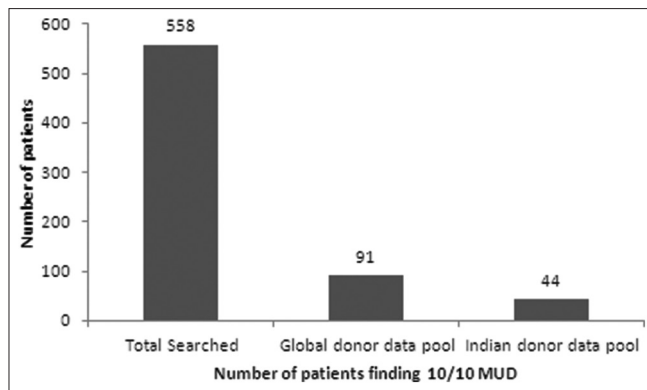


Figure 2: Number of patients finding 10/10 matched unrelated donor in global and Indian donor data pool

2010, expected to increase up to 132,574 in 2020.^[9] Besides each year, around 20 million carriers and 10,000 children are born with thalassemia major in India.^[2] As a standard care of treatment, there seems to be a crucial need to take the dutiful initiatives to increase the number of volunteer donors to make the suitable HLA–MUD for the patients who do not have the matched sibling donor.^[10]

Conclusion

At present, patients requiring MUDT in India are more dependent on finding a match outside India. Even if an Indian patient finds an MUD from global donor database, the cost of doing a transplant from outside India is a major detrimental factor because of the costs involved in transporting the stem cells across the borders. We have clearly demonstrated that the chances of finding an Indian donor have increased since the database of Indian donors has increased. This study clearly identifies the need to build a large Indian database that will not only help in increasing the chances of finding an MUD for Indian patients within India but also provide cost-effective treatment to patients. The findings of this study implicate that amplified efforts are needed to increase donor recruitment to create a larger data pool of voluntary stem cell donor in India so that the chances of saving many vital lives will increase by multiple

folds. If MUD becomes available, transplant can be done easily, and this will provide hope of cure especially in the patients who do not have MRD.

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Conflicts of interest

There are no conflicts of interest.

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