Into account AHA when UCBT, we recommend choosing matches as well (see Figure 2). The role of AHA in graft survival (see Figure 1), which was shown in our grafts were associated with significant reduction in mortality from any cause and non-relapse/non-disease progression mortality in transplants matched at >=6/8 versus <6/8 alleles (p = 0.02 and 0.01, respectively). Although decreased in incidence, there was no significant association for graft failure, GVHD or infections. In subgroup comparison using original HLA typing (<3/6 vs >=3/6, <4/6 vs >=4/6, <5/6 vs >=5/6 matches), a significant reduction in mortality from any cause and non-relapse/non-disease progression mortality was seen in those matched at >=5/6 versus <5/6 loci (p<0.05 and 0.01, respectively). Screening for class I and II AHA was available in 27 patients and was positive in 8/14 patients with primary graft failure and 3/13 engrafters and 5/19 non-engrafters. 

Conclusion: HR typing showed an increase in HLA recipient cord disparity in comparison to standard typing. We validated the current standard for UCB selection as >=5/6 grafts were associated with significantly improved overall survival (see Figure 1), which was shown in our >=6/8 HR matches as well (see Figure 2). The role of AHA in graft failure needs to be further tested. In choosing donors for UCBT, we recommend choosing >=6/8 HR match especially when >=5/6 UCB grafts are available and if able, taking into account AHA.

Developing a Haploidentical Transplant Program: An Indian Experience

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Out of an estimated 20,000 patients requiring an allogeneic HCT in India, only 500 odd patients receive one. Keeping in cognizance the resource constraints, the major reason for the discordance lies in the lack of alternate donors. Whilst unrelated donor marrow and cord suffice for the ethnic majorities in Europe and the USA, such registries provide for less than 10% of HCT recipients due to both cost and an available match. With this background, we initiated a Haploidentical Family Donor HCT program in 2011.

In our initial screening of 50 patients referred for an allogeneic BMT, a matched family donor was available in 11 patients and a suitable Haploidentical family donor was available for 49, whereas a fully matched unrelated donor (10/10) was available for none. Hence we decided to develop a Haploidentical BMT program within the available resources. We chose a Posttransplant Cyclophosphamide (PTCY) based approach with PBSC as the graft source.

We have carried out 40 transplants in 32 patients over the last 3 years (AML-15; ALL-2; CML-BC-2; Lymphoma-2; Severe Aplastic Anemia (SAA)-10; Thalassemia-1). All received PBSC with PTCY on days 3 and 4 followed by cyclosporine and MMF. The conditioning regimen comprised of Fludarabine 150 mg/CY-30 mg/Melphalan-100 mg (SAA) or 120-140 mg (others) with Fludarabine and IV Busulfan (6.4-9.6 mg/kg) or Treosulfan 10-12 gm/m². 2GV TBI was offered to 4 patients instead of Melphalan. Sirolimus was added later on day –7 pretransplant to the last 5 patients with SAA.

30/32 patients surviving beyond 21 days had successful engraftment with full donor chimerism, including 10/11 patients with SAA and Thalassemia. 6/8 evaluable patients undergoing a second Haploidentical HCT engrafted as well. Acute GVHD grade 2-4 developed in 3/32 patients. Day 100 NRM was 5/32 (15%) and the overall survival at 2 years was 55%. The major cause of NRM was infection with Carbapenem-resistant Gram Negative Bacilli accounting for 90% of the deaths. Chronic GVHD occurred in 10% of the evaluable patients. With stringent monitoring for CMV and preemptive therapy, only 1 patient succumbed to CMV disease. The outcome and cost of this extremely high risk group of patients were comparable to matched family donor BMT. PBSC as graft source was associated with a low incidence of both acute and chronic GVHD. We also studied the effect of Natural Killer Cell Ligand Mismatch (NKLMM) donor on the outcome in all our patients. NKLMM was associated with reduced incidence of relapse in patients with hematological malignancies (p=0.03). However, NKLMM donor was associated with poor outcome in patients with SAA (p=0.05).

In summary, Haploidentical HCT based on PTCY and PBSC graft is feasible and probably the most viable form of alternate donor HCT in resource constrained settings with outcomes comparable to matched donor HCT.

Impact of HLA-Mismatch in Unrelated Donor Hematopoietic Stem Cell Transplantation: A Comprehensive Meta-Analysis

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Background: Mismatched unrelated donor (MMURD) transplantation is widely used in patients who lack a matched unrelated donor (MUD). Despite several published observational studies, the magnitude of risk associated with 9 out of 10 MMURD transplant and that of HLA-specific mismatches is still unclear. We performed a meta-analysis to...