Haploidentical transplantation with TCR Alpha/Beta depletion in Pediatric thalassemia after pre transplant immunosuppression

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Aim: Haploidentical hematopoietic stem cell transplantation (Haplo-HSCT) is an option for treating patients who lack a full matched donor. Recent advances in graft engineering with ex vivo T cell depletion of GvHD causing subsets and adoptive immunity transfer with memory (CD45RO) cells has significantly improved the outcome of haplo- HSCT. Our aim was to examine the outcomes of haplo- HSCT using T-cell depleted grafts in children with thalassemia major.

Methods: This is a retrospective study conducted in a tertiary care centre in pediatric patients with thalassemia major who had no full matched donor available. Data of patients undergoing T cell depletion were analyzed from January 2016 to February 2021. The stem cell product underwent ex vivo manipulation with depletion of CD19 or CD45RA along with TCR $\alpha\beta^+$ depletion. Patients with CD45 RA depletion were given sequential donor lymphocyte infusions (DLI) of CD45 RO cells post-transplant.

Results: Thirty-one patients with a median age of transplant being 69 months (range, 21-148 months) were enrolled. Twenty patients (64%) underwent TCR αβ with CD45 RA depletion and the rest 11 patients (36%) underwent CD19 depletion. All patients received pre transplant immunosuppressive (PTIS) treatment prior to transplant. All patients underwent myeloablative conditioning with majority receiving Fludarabine, Busulfan, ATG and Cyclophosphamide. Mean CD34 cell dose and TCR αβ cell dose was 17 x 10^6/kg and 0.017 x 10^6/kg respectively. The median time for neutrophil and platelet engraftment was 12 days for each. Sinusoidal obstruction syndrome (SOS) was seen in 13 (41%) patients with 3 patients having severe SOS.

The incidence of CMV, adenovirus, HSV and BK virus reactivation were 26%, 6%, 3% and 10% respectively. None of the patients developed CMV or adenovirus disease. All patients with BK virus had hemorrhagic cystitis. Bacterial infections with positive blood culture were seen in 3 (10%) patients. No invasive fungal infections were observed in this study group.

Acute GvHD was seen in 9 patients (Grade I/II and Grade III/IV was 7 (22%) and 2 (6%) patients respectively). None of the patients developed chronic GvHD.

Mixed chimerism was observed in 5 patients. One patient had primary rejection and rest of the patients attained complete chimerism after reducing the immunosuppression and DLI was

given to 2 patients. Almost all patients had NK cell and CD4 cell recovery at day 21 and 3 months post-transplant respectively.

Four patients died in this study. The day 100 post-transplant survival was 93.5%. The overall adjusted survival was 87% with a median follow up of 48 months.

Conclusions: T cell depleted transplant after PTIS has improved the transplant outcomes by reducing the risks of GvHD and graft failure.

No conflict of interest to disclose.

Figure 1: Death-censored overall survival of pediatric Thalassemia patients who underwent T cell depletion

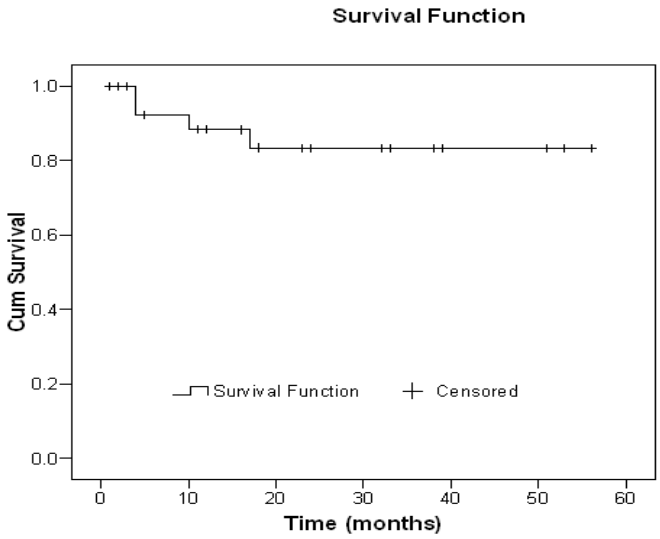

Table 1

Characteristics	**n (%)**
Total number of patients	31 total Male/ Female: 18 (58.1%) / 13 (41.9%)
Thalassemia Class Class 1 Class 2 Class 3	 6 (19.3 %) 22 (71.0%) 3 (9.7%)
Pre- transplant immunosuppression 3 courses/ 2 courses	 28 (90.3) / 3 (9.7)
Median day of Neutrophil engraftment	12 (IQR; 10, 20)
Median day of Platelets engraftment	12 (IQR; 10, 16)
Chimerism >95%	26 (83.8%)
Acute GVHD	Total: 9 (29%) Grade III/IV: 2 (6%)
Viral infections	CMV (26%) adenovirus (6%), HSV (3%) and BK (10%)
Overall survival and mortality	27 (87%) and 4 (12.9%)

IQR; 25th and 75th percentile (interquartile range)