patients. NM conditioning consisted of fludarabine 90 mg/m$^2$ plus 2 Gy TBI, while MA conditioning was cyclophosphamide 120 mg/m2 in combination with 12 Gy TBI or 12.8 mg/kg busilvex. MA conditioning was given to 122 patients and NM to 85 patients. Median age at transplant was 39 (range 15-56) in MA patients and 59 (range 27-73) in NM patients. Donor source, cytogenetic risk, CMV antigen status recipient/donor, sex match, Karnofsky score, and body mass index were not different among MA and NM patients. Disease stages CR1, CR2, and >CR2/Primary Induction Failure (PIF) were analyzed separately. Survival of patients with advanced stage (>CR2/PIF) was short in both groups; 6.1 and 5.2 months in MA and NM, respectively. Patients in CR1 and CR2 were analyzed in details. Patient numbers in MA and NM transplants were 60 vs. 62 in CR1 and 50 vs. 17 in CR2. In CR1 and CR2 MA patients 68% and 48% received bone marrow, whereas all of the NM patients received peripheral stem cells, $P < .001$. Day 100 TRM in MA vs. NM transplants was 8.3% vs. 1.6% in CR1patients and 14% vs. 5.9% in CR2 patients, which was not significantly different. Relapse incidence was comparable among the MA and NM transplants, both in CR1 and CR2 patients. The cumulative incidence of relapse at 1 year was 18.4% (CI: 5.0-28.2) versus 20.9% (CI: 5.2-31.1) in MA and NM patients transplanted in CR1, and 14.5% (CI: 5.1-24.5) versus 11.8% (CI: 0- 27.1) in CR2 patients (n.s.). The 5 year overall survival (OS) probability in the CR1 patients with MA conditioning vs NM conditioning was 63.9% (CI:51.4-76.4) vs 64.0% (CI:51.4-76.6), and among CR2 patients 51.2% (CI:36.0-66.4) vs 64.7 (CI:41.9-87.4), (n.s.). The median survival follow-up time was 55 months (range: 9-137) among CR 1 patients, and 54 months (range: 7-133) among CR2 patients. The 3-year cumulative incidence of chronic GVHD in CR1 patients was 52.8% (CI:39.9-65.8) and 41.9% (CI:29.3-54.7) in MA and NM patients, respectively. In CR2 patients, the incidences were 32.7% (CI:19.0-46.3) and 41.2% (CI:17.8-64.6). In conclusion, OS, TRM and relapse in NM transplants were comparable to MA transplants despite a truly NM regimen and a substantial age difference between groups.

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### Outcomes of Children with Hematologic Malignancies Who Relapse After Allogeneic Hematopoietic Cell Transplantation (AlloHCT)

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**Background:** Relapse is the primary cause of treatment failure after alloHCT for hematologic malignancies. We describe the presentation, management, and outcomes of children with post-HCT relapse, specifically focusing on post-HCT minimal residual disease (MRD), to improve monitoring and intervention strategies.

**Design:** This was a single institution, retrospective cohort study of children with relapse or progression of acute lymphoblastic leukemia (ALL), acute myelogenous leukemia (AML), mixed phenotypic acute leukemia (MPAL) or myelodysplastic syndrome (MDS) post-alloHCT between January 1, 2003 and December 31, 2010. MRD was defined as disease detectable by immunophenotypic, cytogenetic or molecular methods that did not meet classic morphologic criteria for relapse (defined as $\geq$ 5% disease). Relapse was defined as any evidence for disease detected after previously negative results, including MRD. Progressive disease was defined as an increase in any measure from baseline results.

**Results:** 40 of 93 (43%) patients who underwent a first alloHCT experienced relapse, including patients with AML (n=18), ALL (n=16), MPAL (n=4) and MDS (n=2). The median time from alloHCT to relapse was 144 days (range 1 month-58 months). Nine patients with post-HCT MRD as the first evidence for relapse, presented at a median time of 35 days post-HCT (range 28-182 days), with the majority having rapid progression of disease. Median survival after relapse was 123 days (range 4 days-5 years). Estimated 6-month and 1-year post-relapse survival was 30% and 17.5%, respectively. Five of 40 (12.5%) patients are currently alive with a median follow-up of 39 months, including 1 patient with active disease. 1 survivor had MDS and presented with MRD alone. The remaining 4 (with leukemia) presented with overt disease between 146 and 411 days post-HCT. 3 of 5 survivors underwent a second HCT. 11 patients who were able to undergo a second transplant, experienced a 3-year 27% OS starting after relapse. (Figure 1). No patients with AML survived after relapse.

**Conclusion:** Although pre-emptive treatment of relapse in the setting of MRD is felt to be ideal, it may not be feasible. In our study, patients with MRD presented very early post-HCT at a time when complications can be high and therapeutic options are limited. Once MRD was detected, disease progression was rapid limiting the chance to respond to frontline immunotherapeutic options. Accordingly, there was no survival advantage for pediatric patients with leukemia whose relapse was detected as MRD compared to overt disease. Given the poor outcomes of post-HCT relapse and limited ability to treat relapse at the stage of MRD, efforts should focus on developing effective therapies for relapse prevention by identifying those at highest risk of relapse as candidates for novel methods to enhance efficacy of alloHCT.

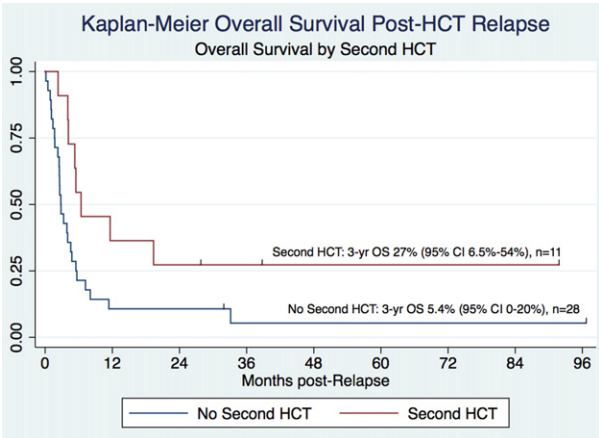


**Figure 1.** OS by Second HCT for Patients with Post-HCT Relapse

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### Primary Hemophagocytic Lymphohistiocytosis and Hematopoeitic Stem Cell Transplantation in Iran

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