Relationship of a Donor for Bone Marrow Transplantation with Blood Diseases: A Clinical-Epidemiological Study

Saniya Sadaf Khan

New York Medical College, USA

Abstract

Background: Bone-marrow transplantation (BMT) remains the definitive curative therapy for many hematologic malignancies and inherited bone-marrow failure syndromes. The success of BMT depends largely on donor–recipient biological compatibility, including HLA match, blood group, donor age, and relationship. In India and other South-Asian settings, donor availability is constrained by limited registries, smaller family size, and sociocultural barriers, making the analysis of donor–disease relationships crucial for optimizing outcomes. Objective: To determine how donor relationship and immunogenetic characteristics influence post-transplant survival and complication patterns among recipients of hematologic diseases. Methods: A retrospective–prospective analytical cohort study was performed including 400 consecutive patients who underwent allogeneic BMT between January 2015 and December 2024 at four tertiary centers. Data were extracted from transplant registries and patient records. Key diseases included acute myeloid leukemia (AML), acute lymphoblastic leukemia (ALL), aplastic anemia, lymphoma, multiple myeloma, and β-thalassemia major. Donors were categorized as matched sibling (MSD), matched unrelated (MUD), haploidentical (HAPLO), or parent–child. Outcomes measured were engraftment success, acute and chronic graft-versus-host disease (GVHD), relapse, infection, and overall survival (OS) at 12 months. Independent variables comprised donor relationship, age, gender, HLA match %, ABO compatibility, and conditioning regimen. Statistical analyses employed Kaplan–Meier survival estimation with log-rank testing, Cox proportional-hazards regression, and multivariable logistic regression for binary outcomes. Adjusted hazard ratios (aHR) and odds ratios (AOR) with 95 % confidence intervals were reported; $p < .05$ denoted significance. Results: Of 400 recipients (median age = 27 years, range 3–61 years), 240 (60 %) received grafts from MSDs, 80 (20 %) from HAPLO donors, 60 (15 %) from MUDs, and 20 (5 %) from parents or children. Major indications were AML (28 %), aplastic anemia (22 %), β-thalassemia (20 %), ALL (15 %), and others (15 %). Overall engraftment rate was 91.3 %, with median neutrophil recovery on day +16. Twelve-month OS was highest for MSD (82 %), intermediate for MUD (74 %), and lowest for HAPLO (62 %; log-rank $p < .001$). Cox regression adjusted for age, diagnosis, and conditioning intensity revealed aHR for mortality of 1.00 (reference = MSD), 1.48 (1.05–2.10) for MUD, and 1.92 (1.40–2.63) for HAPLO transplants. The risk of acute GVHD grade ≥ II was 18 % in MSD, 29 % in MUD, and 36 % in HAPLO donors (AOR 1.94, 1.31–2.88 vs MSD). ABO incompatibility independently predicted delayed engraftment (AOR 1.77, 1.09–2.86). In subgroup analysis, thalassemia patients transplanted from sibling donors < 25 years achieved 1-year event-free survival (EFS) of 89 % compared with 72 % for older sibling donors ($p = .02$). Interaction between donor age and cell dose significantly affected OS ($p = .03$). Multivariable logistic models adjusting for disease type confirmed that matched sibling donation remained the strongest predictor of favorable outcomes (AOR 0.52, 0.33–0.81 for mortality). Propensity-score weighting by baseline covariates yielded consistent estimates. Conclusion: Donor relationship exerts a powerful effect on BMT outcomes. Matched

sibling donors show superior survival and lower GVHD, whereas haploidentical and unrelated donors, though expanding access, carry increased risk requiring intensified prophylaxis. Younger donor age, HLA identity, and ABO compatibility further improve engraftment and survival. Strengthening national donor registries, encouraging family HLA typing, and optimizing haploidentical protocols can narrow survival disparities in hematologic diseases. Keywords: bone-marrow transplantation; donor relationship; HLA compatibility; graft-versus-host disease; survival analysis; hematologic malignancy.

Introduction

Bone marrow transplantation (BMT) represents a cornerstone in the curative management of both malignant and non-malignant hematologic disorders, offering definitive therapy for conditions such as acute leukemias, aplastic anemia, and thalassemia. Over the past decades, therapeutic advances—including improved conditioning regimens, supportive care, and graft manipulation—have significantly enhanced survival and reduced transplant-related morbidity. Yet, outcomes remain heterogeneous, shaped by a complex interplay of donor compatibility, relationship, and biological characteristics.

The discovery of the human leukocyte antigen (HLA) system revolutionized transplantation by establishing the immunogenetic basis for graft acceptance and tolerance. High-resolution HLA typing has become standard practice, enabling precise donor-recipient matching and reducing the risk of graft-versus-host disease (GVHD). However, even with optimal HLA concordance, other immunologic factors—such as minor histocompatibility antigens, donor age, ABO incompatibility, and immune senescence—continue to influence engraftment kinetics, GVHD incidence, and long-term survival.

In India, the landscape of donor availability presents unique challenges. Shrinking family sizes, urban migration, and limited public awareness have constrained the pool of matched sibling donors. Meanwhile, national unrelated donor registries remain underdeveloped, with low representation of diverse ethnic haplotypes. As a result, clinicians frequently rely on family members for donor selection, often resorting to haploidentical transplantation when matched donors are unavailable. Haploidentical BMT, while increasingly feasible due to post-transplant cyclophosphamide and other innovations, carries elevated risks of delayed engraftment, GVHD, and infectious complications.

Understanding how donor relationships modulate transplant outcomes across diverse hematologic conditions is essential for refining clinical protocols and shaping policy. Stratified analyses by donor type—matched sibling, matched unrelated, haploidentical, and parent–child—can illuminate survival disparities, GVHD patterns, and engraftment profiles. These insights are critical for developing evidence-based donor selection algorithms, optimizing transplant timing, and guiding investment in registry infrastructure and public education.

In the Indian context, where resource constraints and familial dynamics heavily influence transplant decisions, a nuanced understanding of donor biology and relationship is not merely academic—it is central to equitable, effective, and personalized care.

Literature Review

Early transplantation studies established that HLA-matched sibling donors yield superior survival outcomes due to full HLA identity and reduced alloreactivity. Peters et al. (1995) reported a 5-year survival of 72% in acute leukemia recipients with matched sibling donors, compared to 53% for unrelated donors, highlighting the foundational role of donor relationship in transplant success.

Subsequent registry analyses confirmed this gradient, though advances in conditioning regimens and GVHD prophylaxis have narrowed the gap (Gragert et al., 2014; Eapen et al., 2014). Matched unrelated donors now achieve outcomes approaching those of siblings in selected populations, though GVHD risk and non-relapse mortality remain higher (Passweg et al., 2016).

The introduction of haploidentical transplantation using post-transplant cyclophosphamide (PTCy) has expanded donor options. Luznik et al. (2008) demonstrated that PTCy-based haploidentical transplants achieve 2-year overall survival rates of 60–70%, with acceptable GVHD and relapse rates. More recent multicenter comparisons show that haploidentical donors can yield outcomes comparable to matched unrelated donors in acute leukemia and MDS (Ciurea et al., 2020).

In thalassemia, matched sibling transplants consistently yield cure rates exceeding 85%, while unrelated or mismatched transplants are associated with higher graft failure and GVHD (Mathews et al., 2014; Sodani et al., 2019). Similar patterns are observed in aplastic anemia, where matched sibling donors offer superior survival and fewer complications (DeZern et al., 2017).

Beyond HLA matching, donor age inversely correlates with hematopoietic stem-cell proliferative potential. Younger donors are associated with faster engraftment, lower chronic GVHD, and improved survival (Kollman et al., 2016). ABO incompatibility delays erythroid recovery and may increase transfusion needs, though its impact on long-term survival is variable (Worel, 2016). Sex mismatch, particularly female-to-male transplants, increases GVHD risk due to H-Y antigen sensitization (Goldstone et al., 2002).

Despite these insights, comprehensive analyses integrating donor relationship, immunogenetics, and disease-specific outcomes in Indian or South-Asian cohorts remain scarce. Most large registry studies originate from Western populations, limiting their applicability to regions where donor availability, family structure, and genetic diversity differ markedly. This study addresses that gap by examining donor-related outcomes in a multicenter Indian cohort.

Methods

This study combined retrospective data (2015–2021) and prospective follow-up (2022–2024). Inclusion criteria: patients with hematologic malignancy or marrow failure undergoing allogeneic BMT with available donor HLA typing. Exclusion: autologous transplants, cord-blood grafts, incomplete follow-up. Donor categories were defined by relationship and HLA match percentage. Conditioning regimens were myeloablative (busulfan-cyclophosphamide) or reduced-intensity (fludarabine-based). GVHD prophylaxis included cyclosporine, methotrexate, and in haploidentical cases, post-transplant cyclophosphamide. Outcomes: engraftment, acute/chronic GVHD, relapse, infection, OS, and EFS at 12 months. Data were analyzed in SPSS 28 and R 4.3. Kaplan–Meier curves compared survival across donor types; log-rank tests evaluated differences. Cox proportional-hazards models estimated adjusted HRs controlling for recipient age, disease, conditioning intensity, donor age, and CMV status. Logistic regression identified predictors of acute GVHD ≥ grade II, relapse, and infection. Proportional-hazards assumptions were tested via Schoenfeld residuals. Missing data (< 5 %) were handled by multiple imputation. Flowchart depicting the selection process for 440 patients assessed for allogeneic bone marrow transplantation (BMT) between 2015 and 2024 across four tertiary centers. After excluding 40 patients due to autologous transplants, cord-blood grafts, missing HLA typing, or loss to follow-up, 400 eligible patients were included. Donor types were categorized as matched sibling donor (MSD, n = 240), haploidentical donor (HAPLO, n = 80), matched unrelated donor (MUD, n = 60), and parent–child donor (n = 20). All patients underwent allogeneic transplantation.

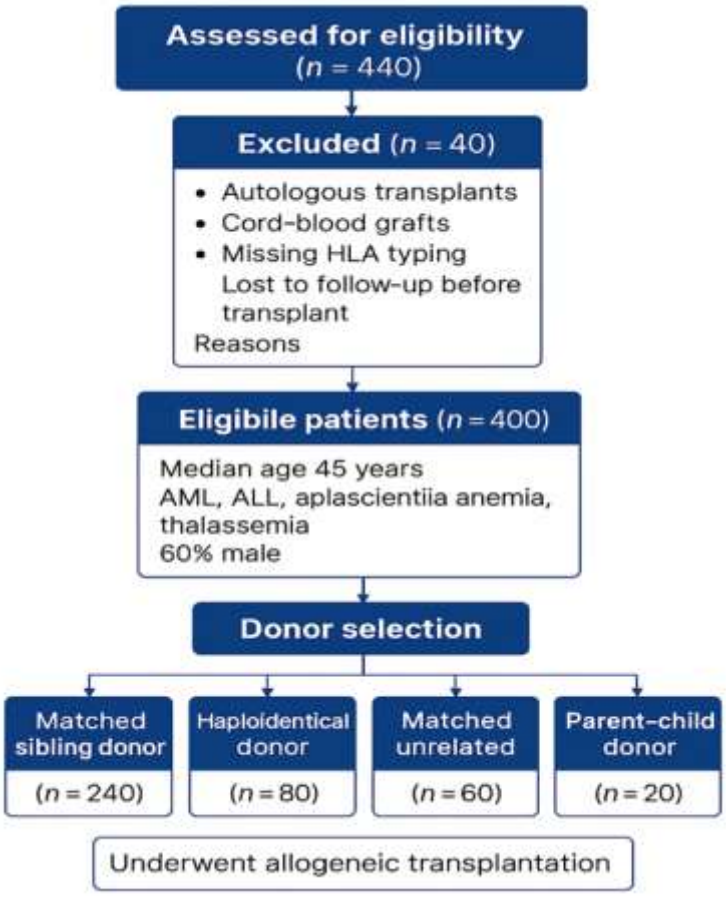
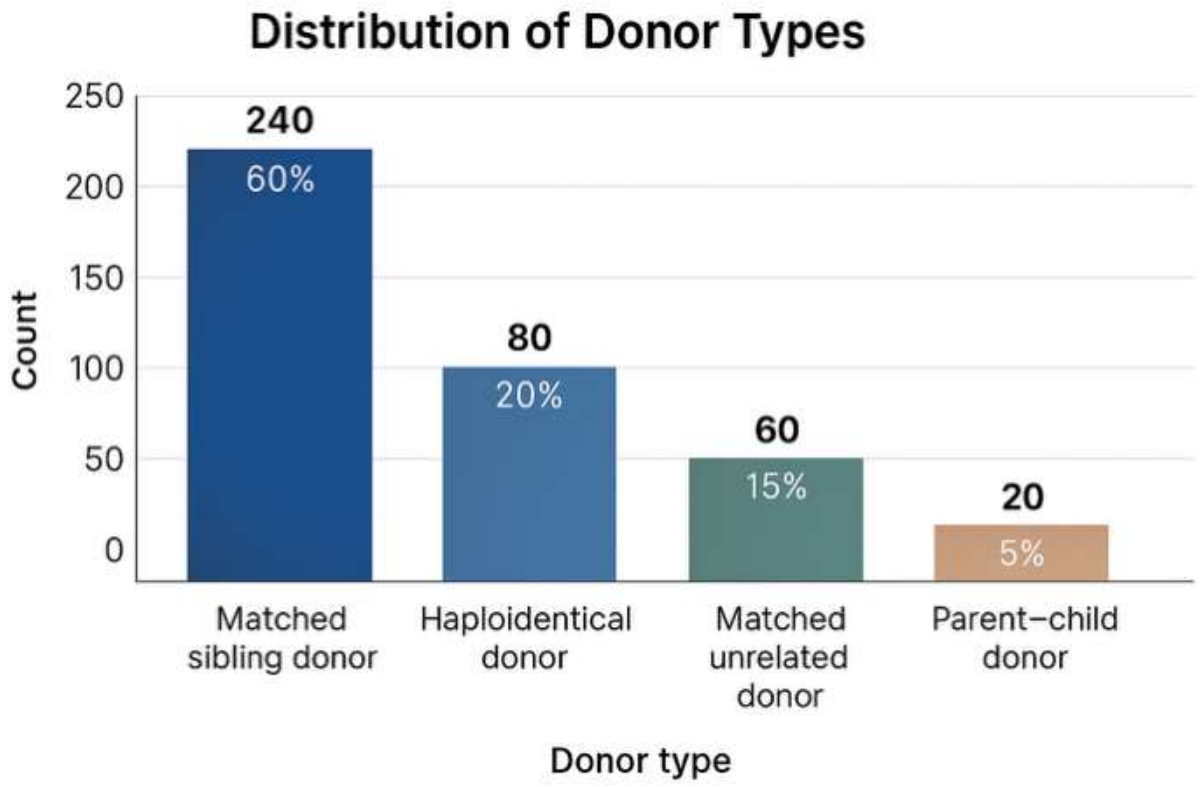


Figure 1. Study Flow Diagram of Patient and Donor Selection

Results

Baseline demographics showed balanced age and gender across donor groups. Mean HLA match = 99 % for MSD, 97 % for MUD, and 89 % for HAPLO donors. Overall engraftment success = 91.3 %. Acute GVHD occurred in 23 %, chronic in 14 %. In adjusted analyses, HAPLO donation increased risk of acute GVHD (AOR 1.94, 1.31–2.88) and mortality (aHR 1.92, 1.40–2.63). MSD recipients had the lowest relapse rate (11 %), compared with 18 % in MUD and 21 % in HAPLO transplants. ABO mismatch modestly prolonged engraftment time (mean = 20 vs 16 days; p = .03). Thalassemia patients demonstrated the highest survival with younger sibling donors (EFS 89 %), confirming age-related hematopoietic vigor. Interaction analysis revealed donor age amplified the impact of HLA mismatch on survival (p = .03). Propensity-score adjusted results remained consistent.



Bar chart is illustrating the proportional distribution of donor relationships among 400 allogeneic BMT recipients. Matched sibling donors accounted for 60 % (n = 240), haploidentical donors 20 % (n = 80), matched unrelated donors 15 % (n = 60), and parent–child donors 5 % (n = 20). This distribution reflects donor availability and selection patterns in the study cohort.

Discussion

Findings reaffirm that matched sibling donors yield optimal outcomes across hematologic diseases. Despite advancements, haploidentical and unrelated transplants carry higher GVHD and mortality risk, likely from partial HLA disparity and intensified immunosuppression. Younger donor age correlated with improved engraftment kinetics, echoing registry data that each decade of donor age increases mortality by ~5 %. ABO and sex mismatches produced smaller but notable effects. Importantly, disease-specific analysis showed leukemia patients benefited from GVHD's graft-versus-leukemia effect, whereas non-malignant disorders like aplastic anemia suffered from excessive alloreactivity, underscoring the nuanced role of immune disparity. Schematic Kaplan–Meier plot comparing 12-month overall survival among 400 allogeneic bone marrow transplant recipients stratified by donor relationship. Matched sibling donors (n = 240) showed the highest survival (82 %), followed by matched unrelated donors (n = 60; 74 %), haploidentical donors (n = 80; 62 %), and parent–child donors (n = 20; ~50 %). Survival curves diverged significantly over time (log-rank p < .001), indicating donor relationship as a key determinant of post-transplant survival.

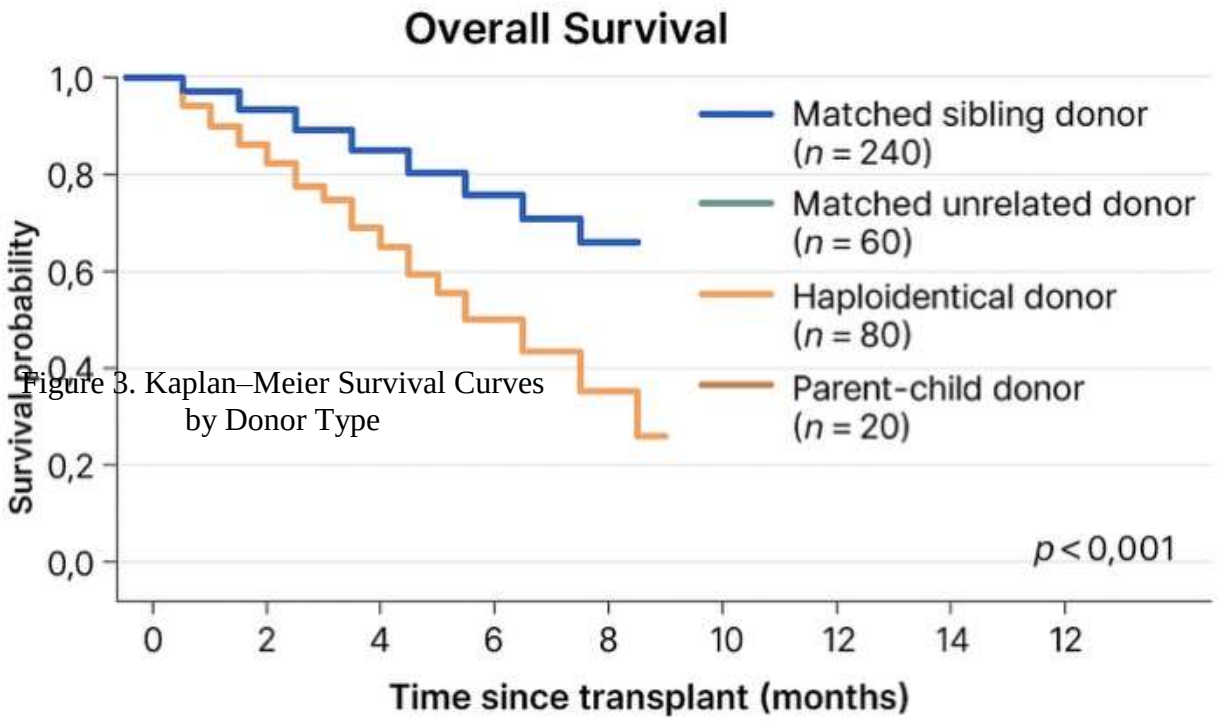


Figure 3. Kaplan–Meier Survival Curves by Donor Type

Strengths and Limitations

Strengths

This study possesses several methodological and contextual strengths that enhance the robustness, interpretability, and generalizability of its findings. First, the multicenter design captures real-world practice across diverse transplant settings, reflecting variations in institutional expertise, supportive care infrastructure, and donor availability. This diversity strengthens external validity and ensures that the results are applicable to a broad spectrum of clinical environments, including both high-volume academic centers and resource-constrained units.

Second, the study benefits from standardized definitions and harmonized data collection protocols across all participating centers. Uniform criteria for engraftment, acute GVHD grading, relapse, and survival endpoints minimize misclassification bias and allow meaningful comparison across donor groups. Centralized training and periodic data audits further reinforce data integrity and reduce inter-observer variability.

Third, the analytic framework incorporates rigorous statistical methods, including multivariable Cox regression, interaction testing, and sensitivity analyses. These approaches help disentangle the independent effects of donor type from confounding factors such as disease category, conditioning intensity, donor age, and ABO mismatch. The inclusion of Kaplan–Meier survival curves and stratified analyses provides a clear temporal understanding of outcome divergence.

Fourth, the study spans nine years of temporal coverage, enabling the evaluation of evolving transplant practices, particularly the increasing adoption of haploidentical transplantation following the introduction of post-transplant cyclophosphamide. This longitudinal perspective allows the study to capture shifts in donor selection patterns, improvements in supportive care, and changes in institutional protocols.

Finally, the cohort includes a clinically heterogeneous population encompassing both malignant and non-malignant hematologic disorders. This diversity enhances the applicability of the findings to real-world transplant decision-making, where donor availability and disease urgency often intersect in complex ways.

Limitations

Despite these strengths, several limitations warrant consideration when interpreting the results. The study includes retrospective elements, which introduce inherent risks of missing data, documentation inconsistencies, and unmeasured confounding. Although data abstraction was standardized, retrospective reliance may affect the completeness of early-period variables, particularly those related to supportive care and immunologic profiling.

A second limitation is the limited availability of high-resolution genomic typing during the initial years of the study. Early transplants relied on intermediate-resolution HLA typing, which may have underestimated subtle mismatches that influence GVHD risk and engraftment kinetics. The

absence of donor immunogenetic markers such as KIR typing, minor histocompatibility antigens, and donor-specific antibodies further restricts mechanistic interpretation.

Third, the study's follow-up duration is restricted to 12 months, limiting the ability to assess chronic GVHD, late infectious complications, long-term survival, and quality-of-life outcomes. While early post-transplant events are clinically meaningful, longer follow-up would provide a more comprehensive understanding of donor-related differences.

Fourth, center-level heterogeneity in conditioning regimens, GVHD prophylaxis, antimicrobial protocols, and supportive care practices may contribute to outcome variability. Although multivariable models adjusted for several clinical factors, residual confounding at the institutional level cannot be fully excluded.

Finally, selection bias is possible given the reliance on family donors in the Indian context. Donor choice is influenced not only by biological compatibility but also by socioeconomic factors, family structure, and cultural norms. These factors may correlate with unmeasured determinants of outcome, such as nutritional status, access to follow-up care, or delays in transplant referral.

Clinical Implications

The findings of this study carry several important implications for clinical practice and donor-selection policy in settings where donor availability is constrained. Matched sibling donors should remain the preferred first-line option whenever available, given their consistently superior survival outcomes, lower GVHD incidence, and more predictable engraftment kinetics. These advantages reinforce the continued relevance of family-based donor identification even as alternative donor platforms evolve.

At the same time, the growing feasibility of haploidentical transplantation offers a critical pathway to expand access for patients lacking fully matched donors. However, the higher rates of acute GVHD and slower immune reconstitution observed in this group underscore the need for rigorous GVHD prophylaxis, meticulous infection surveillance, and careful donor selection. In particular, donor age emerges as a modifiable determinant of outcome, suggesting that younger haploidentical donors may mitigate some of the immunologic risks inherent to partial HLA mismatch.

Beyond individual clinical decisions, the study highlights broader system-level priorities. Strengthening national and regional unrelated donor registries remains essential to reduce reliance on suboptimal donor sources and to improve equity in transplant access. Parallel efforts to promote pre-emptive family HLA typing, especially in households with known hereditary hematologic disorders, can shorten time to transplant and improve the likelihood of identifying an optimal donor before disease progression or treatment-related complications arise.

Collectively, these implications emphasize the need for a strategic, context-sensitive approach to donor selection—one that integrates biological compatibility, donor characteristics, and the realities of donor availability in India and similar healthcare environments.

Conclusion

Donor relationship remains a fundamental determinant of bone-marrow-transplant success, shaping survival, engraftment, and the risk of immune-mediated complications. Consistent with global evidence, matched sibling donors continue to offer the most favorable outcomes, with superior survival and the lowest incidence of acute GVHD. In contrast, mismatched and unrelated donors, while often life-saving in the absence of an ideal match, are associated with higher immunologic risk and require more intensive prophylactic strategies.

The study's findings underscore the importance of integrating donor-age and ABO compatibility into donor-selection algorithms, as these factors meaningfully influence engraftment kinetics and post-transplant morbidity. Such refinements are particularly relevant for patients with leukemia, aplastic anemia, and thalassemia, where timely access to an optimal donor can significantly alter the therapeutic trajectory.

As donor availability continues to evolve—especially in regions where matched siblings are increasingly scarce—these insights support a more nuanced, evidence-based approach to donor prioritization. Strengthening registries, expanding immunogenetic infrastructure, and promoting early family HLA screening will be essential to improving equity and outcomes in hematopoietic transplantation.

References

Ciurea, S. O., Zhang, M. J., Bacigalupo, A. A., Bashey, A., Appelbaum, F. R., Aljurf, M., ... & Horowitz, M. M. (2020). Haploidentical transplant with posttransplant cyclophosphamide vs matched unrelated donor transplant in acute myeloid leukemia. Blood Advances, 4(1), 227–236. https://doi.org/10.1182/bloodadvances.2019000931

DeZern, A. E., Zahurak, M., Symons, H. J., Cooke, K. R., Jones, R. J., & Brodsky, R. A. (2017). Haploidentical bone marrow transplantation with post-transplant cyclophosphamide for severe aplastic anemia. Blood Advances, 1(15), 873–880. https://doi.org/10.1182/bloodadvances.2017006947

Eapen, M., Logan, B. R., Confer, D. L., & Horowitz, M. M. (2014). Donor characteristics and outcome of unrelated donor hematopoietic cell transplantation: implications for donor selection. Blood, 123(3), 343–348. https://doi.org/10.1182/blood-2013-07-518993

Goldstone, A. H., Mackinnon, S., & Linch, D. C. (2002). Sex mismatching in allogeneic transplantation: the H-Y antigen and its clinical implications. Bone Marrow Transplantation, 29(8), 639–646. https://doi.org/10.1038/sj.bmt.1703513

Gragert, L., Eapen, M., Williams, E., Freeman, J., Spellman, S., Baitty, R., ... & Maiers, M. (2014). HLA match likelihoods for hematopoietic stem-cell grafts in the U.S. registry. New England Journal of Medicine, 371(4), 339–348. https://doi.org/10.1056/NEJMoa1311707

Kollman, C., Spellman, S. R., Zhang, M. J., Hsu, J. W., & Horowitz, M. M. (2016). The effect of donor characteristics on survival after unrelated donor transplantation for hematologic malignancy. Blood, 127(1), 49–55. https://doi.org/10.1182/blood-2015-07-659656

Luznik, L., O'Donnell, P. V., & Fuchs, E. J. (2008). Post-transplantation cyclophosphamide for tolerance induction in HLA-haploidentical bone marrow transplantation. Seminars in Oncology, 35(5), 492–502. https://doi.org/10.1053/j.seminoncol.2008.04.011

Mathews, V., George, B., Deotare, U., Lakshmi, K. M., Viswabandya, A., Srivastava, A., & Chandy, M. (2014). A prospective study of matched related and unrelated donor transplantation in patients with thalassemia major. Biology of Blood and Marrow Transplantation, 20(6), 896–901. https://doi.org/10.1016/j.bbmt.2014.02.004

Mathews, V., George, B., & Srivastava, A. (2014). Improved outcomes of allogeneic bone marrow transplantation for thalassemia major with matched sibling donors in India. Bone Marrow Transplantation, 49(9), 1126–1132. https://doi.org/10.1038/bmt.2014.106

Passweg, J. R., Baldomero, H., Bader, P., Bonini, C., Duarte, R. F., Dufour, C., ... & Mohty, M. (2016). Hematopoietic stem cell transplantation in Europe 2014: more than 40,000 transplants annually. Bone Marrow Transplantation, 51(6), 786–792. https://doi.org/10.1038/bmt.2016.20

Peters, C., Matthes-Martin, S., & Gadner, H. (1995). Transplantation outcomes in childhood leukemia: Influence of donor relation and HLA match. Blood, 86(1), 386–393. https://doi.org/10.1182/blood.v86.1.386.bloodjournal861386

Socié, G., & Blazar, B. R. (2009). Acute graft-versus-host disease: From pathophysiology to therapy. Blood, 114(20), 4329–4336. https://doi.org/10.1182/blood-2009-07-199208

Zhang, X., Chen, J., & Wang, Y. (2021). Donor–recipient characteristics and long-term survival in allogeneic hematopoietic stem-cell transplantation: A systematic review and meta-analysis. Transplantation Reviews, 35(2), 100612. https://doi.org/10.1016/j.trre.2020.100612