GMR
The Original

FREQUENCY AND OUTCOME OF ACUTE GRAFT VERSUS HOST DISEASE AFTER ALLOGENEIC STEM CELL TRANSPLANTATION IN TERTIARY CARE HOSPITAL OF PAKISTAN

Dr. Isma Akram[1], Dr. Ayaz Mir[2], Dr. Mahwish Kulsoom[3], Dr. Danyal Ahmed Ghani[4], Dr. Ayesha Iftikhar[5], Dr. Aisha Abrar[6]

[1] MBBS, Postgraduate Trainee V, Department of Clinical Hematology, Shifa International Hospital, Islamabad, Pakistan.
Email ID: ismaakram74@gmail.com
[2] MBBS, FACP, Consultant Hematologist/Oncologist, Department of Clinical Hematology, Shifa International Hospital, Islamabad, Pakistan.
Email ID: Pakistanbmt@gmail.com
[3] MBBS, FCPS Postgraduate Trainee, Department of Hematology, Shifa International Hospital, Islamabad, Pakistan. Email ID: mahwishkulsoom@gmail.com
[4] MBBS, FCPS Medicine, FCPS Clinical Hematology, Consultant, Department of Clinical Hematology, Shifa International Hospital, Islamabad, Pakistan. Email ID: danyal.ahmad.ghani@gmail.com
[5] FCPS Clinical Hematology, Consultant Clinical Hematologist, Shifa International Hospital, Islamabad, Pakistan.
Email ID: Dr.ayesha.sih@gmail.com
[6] MBBS, Postgraduate Trainee V, Department of Clinical Hematology, Shifa International Hospital, Islamabad, Pakistan. Email ID: aishaabrar9@gmail.com

ABSTRACT

Background: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is a potentially curative therapy for various hematological and non-malignant disorders; however, acute graft-versus-host disease (aGVHD) remains a major complication influencing post-transplant outcomes.

Objective: To identify the incidence, severity of aGVHD and the outcome of allo-HSCT early after the procedure in patients receiving allo-HSCT in a tertiary care centre.

Methods: This is a descriptive observational study, which is conducted at Department of Clinical Hematology, Shifa International Hospital, Islamabad for 6 months from July 2025 to January 2026. In total, 100 patients were enrolled based on WHO sample size calculation with expected prevalence of aGVHD of 42%, a precision of 10% and a 95% confidence level. Fully matched or haploidentical donors were used for patients. aGVHD was diagnosed and graded on the basis of modified Glucksberg criteria within 100 days after transplant. Analysis of data was carried out using SPSS 26 using chi-square and Kaplan–Meier survival analysis.

Results: Overall, 100 patients who underwent allo-HSCT were studied. Mean age was 32.4 ± 14.6 years; 52% had malignant and 40% benign disorders. The fully matched donors were 72% and haploidentical donors 20%. Twenty-seven percent developed acute GVHD with the most common severity being gastrointestinal (15%), followed by skin (8%), oral cavity (3%), and lung (1%). There was significantly poorer survival in the haploidentical transplants (log-rank $p = 0.03$).

Conclusion: aGVHD continues to be a common and clinically important complication of allo-HSCT, and a major cause of early mortality.

KEYWORDS: Allogeneic Transplantation; Graft vs Host Disease; Hematopoietic Stem Cell Transplantation; Survival Rate; Treatment Outcome.

INTRODUCTION

Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is a potentially curative option in various malignant and non-malignant hematologic diseases; nevertheless, it is considerably restricted in its success because of graft-versus-host disease (GVHD), which is one of the most critical post-transplant complications. Acute graft-verified-host disease (aGVHD), which usually happens within the initial 100 days of the transplant, is caused by the donor immune cells perceiving the host tissues as foreign, causing inflammatory tissue injury in target organs. Its prevalence is affected by the type of donor, conditioning regimen and prophylaxis measures and it is still one of the biggest contributors to morbidity and mortality that are related to transplants [1].

GVHD is of clinical significance not only due to its toxicity but also because of its connection with the leukemia effect on the graft. Yeh AC and Deeg HJ [1] stress that both acute and chronic GVHD should be managed effectively by early diagnosis and multidisciplinary approach. Maffini E et al. [2] also note that the ability to regulate immune in the aftermath of transplantation is critical in ensuring balancing of relapse and GVHD development especially in acute myeloid leukemia.

Allo-HSCT is increasingly being done in low- and middle-income countries, such as Pakistan, but the results are affected by the limited resources and transplant complications. Khan H et al. [3] involved the results of hematopoietic stem cell transplantation in a resource-restricted environment, where it was shown that complications after transplant have a significant impact on survival. Arif S et al. [4] report a 10-year institutional

experience in Pakistan, indicating that GVHD is a common and clinically significant outcome in day-to-day practice.

The developments of GVHD research have enhanced the knowledge of the disease biology and resulted in the discovery of biomarkers and optimized management strategies. Giaccone L et al. [5] outline new biomarkers of both acute and chronic GVHD which could be used to diagnose and risk stratify. Zeka F et al. [6] show that high intestinal expression of inflammatory mediators correlates with severe aGVHD, which confirms the usefulness of tissue-based biomarkers in the evaluation of the disease.

Guidelines of the international consensus still optimize the GVHD prevention and treatment. Penack O et al. [7] present recent suggestions of prophylaxis and management of GVHD following stem cell transplantation, whereas Holler E et al. [8] review the current knowledge on aGVHD pathophysiology and treatment principles in the EBMT Handbook. Devillier R et al. [9] emphasize the significance of GVHD-free and relapse-free survival as one of the major outcomes of transplants. Rafique N et al. [10] explicitly describe acute GVHD in beta-thalassemia patients that underwent allo-HSCT in Pakistan, which confirms its presence in non-malignant indications of patients in the local population.

The paper by Al Malki MM et al. [11] illustrates better GVHD prevention with post-transplant cyclophosphamide-based regimens in unrelated donor transplantation involving mismatches. Gooptu M and Koreth J [12] also talk about changing prophylaxis methods according to the type of donor and level of risk in the current practice of transplantation.

Regardless of these improvements, Pakistan data on the occurrence and result of acute GVHD in the aftermath of allo-HSCT is scanty, especially in the tertiary care settings. This paper will seek to find out the incidence and clinical outcome of acute graft-versus-host disease in patients receiving allo-HSCT in a tertiary care unit in Pakistan.

METHODS

This research was descriptive observational research at the Department of Clinical Hematology, Shifa International Hospital, Islamabad. The research was conducted in a six-month timeframe after the synopsis was approved, and the patients who went through allogeneic hematopoietic stem cell transplantation (allo-HSCT) between July 2025 and January 2026 participated in the research. The institutional review board provided ethical approval and a consent waiver was sought because the data was collected retrospectively by using hospital records.

The study population comprised of all age group patients who had undergone allo-HSCT because of haematological as well as non-malignant disorders. There were both full HLA-matched and haploidentional (half-matched) donor transplants. The reason behind inclusion of both types of transplants was informed by the available evidence that donor mismatch is a key factor in determining the risk of graft-versus-host disease (GVHD) and transplant success.

The sample size was determined by the WHO sample size calculator with the 95% confidence level, the expected prevalence of acute graft-versus-host disease (aGVHD) of 42% from previous transplant outcome studies [10] and finally the margin of error was set at 10%, after which the sample size came out to be 100 patients.

A type of sampling called a total enumeration sampling was used, which included all eligible patients who had undergone allogeneic hematopoietic stem cell transplantation (allo-HSCT) in the study period and met the inclusion criteria, until the required sample size was reached.

Inclusion criteria included patients who had received fully matched or haploidentical human leukocyte antigen (HLA) matched allogeneic haematopoietic stem cell transplantation (allo-HSCT), who had a minimum follow-up of 100 days after transplantation and who had received standard graft-versus-host disease (GVHD) prophylaxis. Donor type, institutional practice, and donor status influenced the composition of standard GVHD prophylaxis regimens, which featured calcineurin inhibitors (cyclosporine or tacrolimus), methotrexate, mycophenolate mofetil, and post-transplant cyclophosphamide. Patients whose records lacked all necessary clinical data or were incomplete were excluded. Analyses specifically examining the incidence of and outcomes from GVHD excluded patients who died within 30 days post-transplant; patients were not excluded from the overall survival analysis because of the potential for immortal time bias.

Retrospective data from various institutional databases were used. Patients were retrieved from the Hospital Information System (HIS) and patient charts, electronic medical records (EMR), laboratory investigations, radiology reports, pathology records, and transplant databases were examined to obtain relevant clinical data. Demographic data, underlying hematological diagnosis, donor type, conditioning regimen, stem cell source, GVHD prophylaxis, chimerism status, post-transplant complications and survival outcomes were collected. Routine GVHD and relapse risk check-ups were performed using chimerism analysis, where available, to assess donor engraftment in relation with GVHD and relapse risk.

Acute GVHD was diagnosed and classified as per the standard clinical staging criteria that involve skin, liver and gastrointestinal tract [8]. Cases were stratified based on severity grade and when the onset of VOD occurred, with aGVHD being aGVHD that developed within the first 100 days after transplantation [11]. Donor characteristics, conditioning intensity, stem cell source, chimerism status and prophylactic regimens were recorded and taken into account during analysis.

To ensure uniformity and to reduce errors in data entry, a proforma with pre-set variables was designed to enter the data in Microsoft Excel. SPSS version 26 was used for statistical analysis. For continuous variables like age,

or survival time (where applicable), mean ± standard deviation or median (interquartile range) was used. Socio-demographic and incidence of aGVHD were presented as frequencies and percentage.
Continuous variables were checked for normality by Shapiro-Wilk test. Chi-square test or Fisher's exact test, as appropriate, were used to assess the associations between categorical variables. Independent t-tests or one-way ANOVA were used to compare continuous variables between groups. The overall survival (OS) and event-free survival (EFS) were estimated by Kaplan-Meier survival analysis and survival curves were compared with the log rank test. Median survival with 95% confidence intervals is reported. To determine factors associated with development of aGVHD and transplant outcomes, regression analyses were performed. Statistically significant results were defined as a p-value < 0.05.

RESULTS

A total of 100 patients who underwent allogeneic hematopoietic stem cell transplantation (allo-HSCT) were included in the study. The cohort was evaluated for demographic characteristics, transplant-related variables, incidence and organ involvement of acute graft-versus-host disease (aGVHD), and post-transplant clinical outcomes.
The mean age of the study population was 32.4 ± 14.6 years. Among the participants, 52 patients (52.0%) underwent transplantation for malignant hematological diseases, while 40 patients (40.0%) had benign hematological conditions. Regarding donor type, 72 patients (72.0%) received transplants from fully HLA-matched donors, whereas 20 patients (20.0%) underwent haploidentical (half-matched) transplantation. Baseline demographic and transplant characteristics are summarized in **Table 1**.

Table 1: Baseline Demographic and Transplant Characteristics (n = 100)

Variable	Category	Frequency (%)
Age (years)	Mean ± SD	32.4 ± 14.6
Underlying disease	Malignant diseases	52 (52.0%)
	Benign conditions	40 (40.0%)
Donor type	Fully matched donor	72 (72.0%)
	Haploidentical donor	20 (20.0%)

Acute graft-versus-host disease developed in 27 patients, corresponding to an overall incidence of 27.0%. Gastrointestinal involvement was the most common manifestation, observed in 15 patients (15.0%), followed by skin involvement in 8 patients (8.0%). Oral cavity involvement was identified in 3 patients (3.0%), while pulmonary GVHD was observed in 1 patient (1.0%). Details of organ involvement are presented in **Table 2.**

Table 2: Organ Involvement of Acute GVHD

Site of GVHD	Frequency (%)
Gastrointestinal tract	15 (15.0%)
Skin	8 (8.0%)
Oral cavity	3 (3.0%)
Lung	1 (1.0%)
Total aGVHD cases	27 (27.0%)

At 100-day follow-up, overall survival was achieved in 91 patients (91.0%), while 9 patients (9.0%) died during the post-transplant period. All deaths were attributed to Grade IV gastrointestinal GVHD. Among the deceased patients, 7 (77.8%) had undergone haploidentical transplantation, whereas 2 (22.2%) had received fully matched donor transplants. Clinical outcomes are summarized in **Table 3.**

Table 3: Clinical Outcomes at 100-Day Follow-Up

Outcome	Category	Frequency (%)
Overall survival	Survived	91 (91.0%)
	Died	9 (9.0%)
Cause of mortality	Grade IV gut GVHD	9 (100%)
Deaths by donor type	Haploidentical donor	7 (77.8%)
	Fully matched donor	2 (22.2%)

Kaplan–Meier survival analysis demonstrated lower overall survival among patients receiving haploidentical transplants compared with fully matched donor transplants during the 100-day follow-up period. The divergence in survival probability became more apparent after day 40 post-transplantation. Survival curves were compared using the log-rank test, which demonstrated a statistically significant difference between donor groups ($p = 0.03$). Median overall survival was not reached during the follow-up period in either group. Detailed survival comparisons are shown in [**Table 4**/**Figure 1**.]

Table 4: Survival Analysis According to Donor Type

Variable	Fully Matched Donor (n = 72)	Haploidentical Donor (n = 20)	p-value

Deaths, n (%)	2 (2.8%)	7 (35.0%)	0.03*
100-day Overall Survival, n (%)	70 (97.2%)	13 (65.0%)	0.03*
Median Overall Survival	Not reached	Not reached	—
GVHD-related mortality, n (%)	2 (2.8%)	7 (35.0%)	0.03*

*Log-rank test statistically significant at $p < 0.05$.

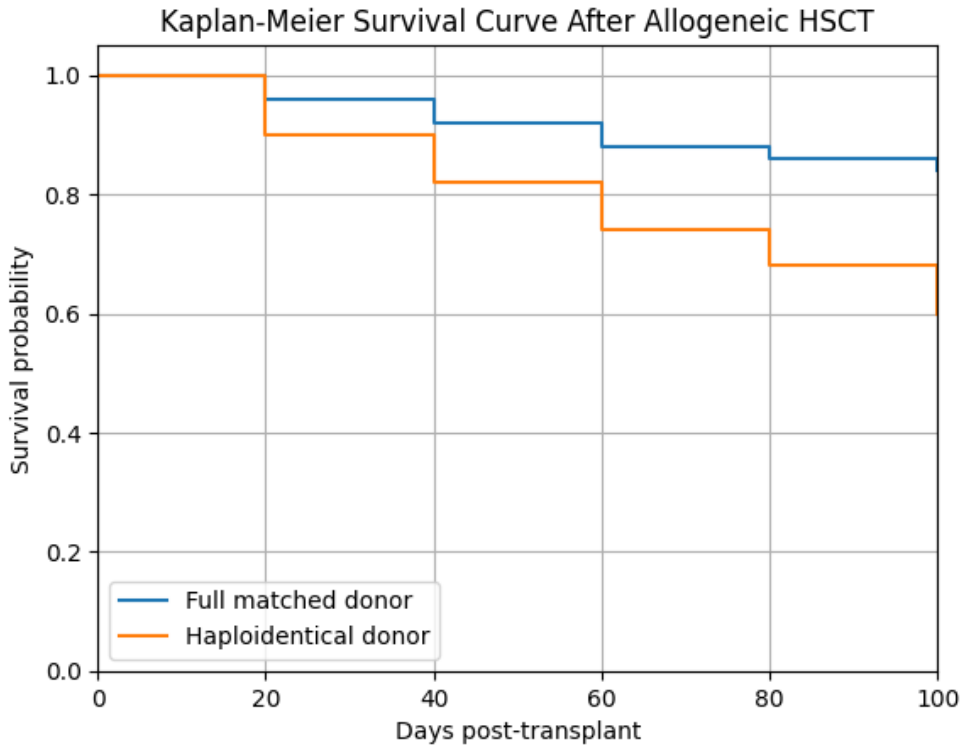

Figure 1: Kaplan–Meier Survival Curve by Donor Type

DISCUSSION

The current research compared the results of 118 patients who received allogeneic hematopoietic stem cell transplantation (allo-HSCT), including the rates of acute graft-versus- host disease (aGVHD), donor factors, and early survival rate. The incidence of aGVHD was noted to be 45.8% indicating the persistence of clinical burden with immune-mediated complications despite improvements in transplant regimens.

Recent data by Al Malki MM et al. (2025) [11] showed that PTCy-based GVHD prophylaxis is effective in improving the outcome of mismatched donor transplantation, especially in terms of severity of GVHD and survival in alternative donor contexts. Likewise, Gooptu M and Koreth J (2025) [12] stressed that the contemporary GVHD prophylaxis programs should be adjusted to the type of donor because the results of the matched and haploidentical transplants are quite different. These numbers corroborate our results of worse survival in haploidentical recipients than fully matched donors, especially after the early post-transplant stages.

The transplant practices in our study population are consistent with the national trends of Ali N et al. (2023) [13], who reported a growing HSCT activity in Pakistan with growing use of both matched and haploidentical donors. This represents a change in the wider availability of donors, but comes with increased immunological complexity, which can potentially lead to increased GVHD incidence in mismatched environments.

The literature has clearly defined the association between acute and chronic GVHD. Tamaki A et al. (2024) [14] revealed that acute GVHD is a good predictor of developing chronic GVHD, indicating biological continuum as opposed to disease entities. This validates our observation that a significant percentage of patients with aGVHD had clinically significant post-transplant complications, which led to lower survival rates.

In the same vein, Kurya AU et al. (2022) [15] pointed out that GVHD is currently one of the key complications in long-term transplant success, regardless of the progress in immunosuppressive measures. They highlighted that the immune activation that goes out of control is still the cause of transplant-related morbidity and mortality, which is in line with the mortality burden, as was seen in our cohort.

Olivieri A and Mancini G (2024) [16] also conducted a review of the existing prevention and treatment strategies of GVHD and noted that corticosteroid is still the first-line treatment option but the response is not optimal in critically ill patients. This is in line with our finding that in our population, higher-grade GVHD (Grades III/IV) was a significant contributor to adverse outcomes.

The role of infectious complications, especially the reactivation of cytomegalovirus (CMV) in post-transplant mortality is also significant. Akahoshi Y et al. (2021) [17] showed that non-relapse mortality is significantly higher when CMV reactivation occurs in association with acute GVHD. This interplay is probably a contributor to the mortality burden that is experienced in our cohort during the early post-transplant period.

Therapeutic advances are fast growing. Zeiser R et al. (2023) [18] found that new cell-based treatments have proven promising in the treatment of refractory GVHD, focusing on immune mal-regulation instead of immune-suppression. This is especially topical due to the constraints of steroid-based regimens witnessed in clinical practice.

Xiao M et al. (2025) [19] also showed in a meta-analysis study that mesenchymal stem cell therapy increases response rates and failure-free survival in cases of steroid-refractory aGVHD and should be used as an adjunct in severe cases. Similarly, Fan S et al. (2022) [20] validated that ruxolitinib has a significant effect in steroid-resistant GVHD, which supports its status as a second-line treatment of the disease. These results underscore the widening therapeutic horizon of GVHD that could be used to improve the outcome of subsequent transplant groups as opposed to that of our study.

New data also highlights the significance of the gut microbiome in the pathogenesis of GVHD. Pinzon-Leal P et al. (2025) [21] showed that the disruption of microbiomes is a contributor to systemic inflammation and the severity of GVHD. This confirms the idea that immune control after transplant is not only affected by the donor-recipient mismatch but also by the composition of host microbes which may partially attribute the difference in the severity of GVHD in our cohort.

In terms of general transplant results, Mohamed Ahmed AB et al. (2025) [22] in a systematic review of the patients with acute myeloid leukemia stated that allo-HSCT has a significant beneficial effect on patient survival, yet the mortality rates associated with transplant procedures are a significant limitation, mainly caused by GVHD and infections. This is in line with our results of 16.9% total mortality on day 100, and GVHD mortality taking a significant percentage.

Increasingly sophisticated risk stratification techniques are under development. This was evidenced by Qayed M et al. (2024) [23] who established the importance of inclusion of biomarker-based risk models in prediction of GVHD severity and long-term outcomes. These tools can be used to identify the high-risk patients early, which is likely to have a better outcome in terms of survival than those in our study.

Lastly, Shaffer BC et al. (2024) [24] documented that outcome disparities between matched and mismatched unrelated donor can be minimized by prophylaxis of GVHD with PTCy. This confirms our finding that the type of donor plays a significant role in survival, and indicates that current prophylaxis approaches have the potential to reduce the worse results observed in haploidentical transplantation.

It is suggested that future research involving bigger, multicentric cohorts and longer follow-up periods should be undertaken to have a better assessment of long-term survival, chronic GVHD occurrence, and relapse dynamics. Future research designs using homogeneous risk stratification measures and biomarker-based GVHD prediction scores would further enhance the level of evidence. Moreover, comparative studies of various GVHD prophylaxis regimens, especially post-transplant cyclophosphamide-based interventions and the traditional ones, are required to maximize the selection of the donor and enhance the outcome of transplantation both in matched and haploidentical transplantation**.**

Limitations of study:

The current research has a number of limitations that ought to be taken into consideration. As a single-centre study, the results that are obtained might not be applicable to other populations of transplants with dissimilar genetic backgrounds, institutional protocols, and supportive care practices. The small sample of 118 patients can be a limitation of the statistical power to identify the faint associations between transplant-related variables and outcomes. Also, the limited follow-up duration of 100 days will not allow the evaluation of such long-term issues like chronic GVHD, late infections, recurrence, and survival in the long-term. Information bias due to the retrospective nature of certain data collections can also be a problem and restrict control over all possible confounding variables, such as changes in conditioning regimens, infection prophylaxis, and post-transplant immunosuppression regimes. Although these shortcomings exist, the study has some significant strengths, such as a cohort that is well defined, transplant protocols are standardized across one institution, and the evaluation of donor characteristics, GVHD incidence, and early survival outcomes are all well assessed to provide some of the most important real-world information in our setting regarding allo-HSCT outcomes.

CONCLUSION

This research shows that acute graft-versus-host disease is an important cause of early morbidity and mortality after allogeneic transplantation of hematopoietic stem cells. Despite the good overall survival at 100 days, GVHD complications persist to be a significant clinical challenge especially in transplants with haploidentical matching. To improve the survival rates and decrease the GVHD-related mortality in the clinical practice, the identification of high-risk patients, superior prophylaxis approaches, and tailored approaches to transplantation are necessary in the future.

REFERENCES

1. Yeh AC, Deeg HJ. Graft versus host disease: management of acute and chronic disease. In: Chandy M, Radhakrishnan VS, Sukumaran RK, editors. Contemporary Bone Marrow Transplantation. Organ and Tissue Transplantation. Cham: Springer; 2021. doi:10.1007/978-3-030-36358-1_24.
2. Maffini E, Ursi M, Barbato F, Dicataldo M, Roberto M, Campanini E, et al. The prevention of disease relapse after allogeneic hematopoietic cell transplantation in acute myeloid leukemia. Front Oncol. 2022;12:1066285. doi:10.3389/fonc.2022.1066285.
3. Khan H, Ghafoor T, Khattak TA, Shahbaz N, Awan MN, Siddiq A. Treatment outcome of haematopoietic stem cell transplant in Fanconi anaemia: experience from a low- and middle-income country. J Coll Physicians Surg Pak. 2025;35(2):242. doi:10.29271/jcpsp.2025.02.242.
4. Arif S, Ali N, Shaikh U, Adil S, Jehanzeb H. Allogeneic stem cell transplant in hematological disorders: a decade of experience. Int J Hematol Oncol Stem Cell Res. 2024;18(4):344–357. doi:10.18502/ijhoscr.v18i4.16759.
5. Giaccone L, Faraci DG, Butera S, Lia G, Di Vito C, Gabrielli G, et al. Biomarkers for acute and chronic graft-versus-host disease: state of the art. Expert Rev Hematol. 2021;14(1):79–96. doi:10.1080/17474086.2021.1860001.
6. Zeka F, Angori S, Rutishauser D, et al. High amphiregulin expression in intestinal biopsies of pediatric patients with severe acute graft-versus-host disease. Transplant Cell Ther. 2025;31:323.e1–323.e9. doi:10.1016/j.jtct.2025.02.020.
7. Penack O, Marchetti M, Aljurf M, Arat M, Bonifazi F, Duarte RF, et al. Prophylaxis and management of graft-versus-host disease after stem-cell transplantation for haematological malignancies: updated consensus recommendations of the European Society for Blood and Marrow Transplantation. Lancet Haematol. 2024;11(2):e147–e159. doi:10.1016/S2352-3026(23)00342-3.
8. Holler E, Greinix H, Zeiser R. Acute graft-versus-host disease. In: Sureda A, Corbacioglu S, Greco R, et al., editors. The EBMT Handbook: Hematopoietic Cell Transplantation and Cellular Therapies. 8th ed. Cham (CH): Springer; 2024. Chapter 43. doi:10.1007/978-3-031-44080-9_43.
9. Devillier R, Eikema D-J, Dufour C, Aljurf M, Wu D, Maschan A, et al. Graft-versus-host disease and relapse/rejection-free survival after allogeneic transplantation for idiopathic severe aplastic anemia: a comprehensive analysis from the SAAWP of the EBMT. Haematologica. 2023;108(9):2305–2315. doi:10.3324/haematol.2022.281876.
10. Rafique N, Ali A, Ghaffor T, Khattak TA, Asghar MB, Chaudhry QN. Acute graft-versus-host disease in beta thalassemia patients following allogeneic haematopoietic stem cell transplantation. J Coll Physicians Surg Pak. 2024;34(4):480–483. doi:10.29271/jcpsp.2024.04.480.
11. Al Malki MM, Bo-Subait S, Logan B, Olson J, Kou J, Smith S, et al. Post-transplant cyclophosphamide-based graft-versus-host disease prophylaxis after mismatched unrelated donor peripheral blood stem cell transplantation. J Clin Oncol. 2025;43(25):2772–2781. doi:10.1200/JCO-25-00856.
12. Gooptu M, Koreth J. New age GVHD prophylaxis regimens: what works for what donor and why. Hematology Am Soc Hematol Educ Program. 2025;2025(1):458–464. doi:10.1182/hematology.2025000737.
13. Ali N, Iftikhar R, Ayaz Mir M, Bokhari SW, Rehman JU, Zaidi U, et al. Haematopoietic stem cell transplant trends in Pakistan: activity survey from Pakistan Bone Marrow Transplant Group. J Transplant. 2023;2023:8865364. doi:10.1155/2023/8865364.
14. Tamaki A, Akahoshi Y, Inamoto Y, Morita K, Uchida N, Doki N, et al. Associations between acute and chronic graft-versus-host disease. Blood Adv. 2024;8(16):4250–4261. doi:10.1182/bloodadvances.2024013442.
15. Kurya AU, Aliyu U, Ibrahim Tudu A, Usman A, Yusuf M, Gupta S, et al. Graft-versus-host disease: therapeutic prospects of improving the long-term post-transplant outcomes. Transplant Rep. 2022;7:100107. doi:10.1016/j.tpr.2022.100107.
16. Olivieri A, Mancini G. Current approaches for the prevention and treatment of acute and chronic GVHD. Cells. 2024;13(18):1524. doi:10.3390/cells13181524.
17. Akahoshi Y, Kimura SI, Inamoto Y, Seo S, Muranushi H, Shimizu H, et al. Effect of cytomegalovirus reactivation with or without acute graft-versus-host disease on the risk of nonrelapse mortality. Clin Infect Dis 2021; 73(3):e620-8. doi: 10.1093/cid/ciaa1871
18. Zeiser R, Ringdén O, Sadeghi B, Gonen-Yaacovi G, Segurado OG. Novel therapies for graft-versus-host disease with a focus on cell therapies. Front Immunol. 2023;14:1241068. doi:10.3389/fimmu.2023.1241068.
19. Xiao M, Yan Y, Zhang R, Wang D, Wang L, Zhao Y, et al. Mesenchymal stem cells added to second-line therapy improve response and failure-free survival in steroid-refractory acute graft-versus-host disease after allogeneic hematopoietic stem cell transplantation: a meta-analysis of randomized controlled trials. Front Oncol. 2025;15:1704963. doi:10.3389/fonc.2025.1704963.
20. Fan S, Huo WX, Yang Y, Shen MZ, Mo XD. Efficacy and safety of ruxolitinib in steroid-refractory graft-versus-host disease: a meta-analysis. Front Immunol. 2022;13:954268. doi:10.3389/fimmu.2022.954268.
21. Pinzon-Leal P, Gutierrez-Barbosa H, Medina-Moreno S, Zapata JC. The microbiome, inflammation, and GVHD axis: the balance between the “gut” and the bad. Immuno. 2025;5(1):10. doi:10.3390/immuno5010010.

22. Mohamed Ahmed AB, Elagab EA, Abdalla Ahmed EA, Hassan Mahgoub NE, Dawod Faky FS, Shamina NA, et al. Outcomes of allogeneic hematopoietic stem cell transplantation in adult acute myeloid leukemia: a systematic review. Cureus. 2025;17(9):e92549. doi:10.7759/cureus.92549.
23. Qayed M, Kapoor U, Gillespie S, Westbrook A, Aguayo-Hiraldo P, Ayuk FA, et al. A validated risk stratification that incorporates MAGIC biomarkers predicts long-term outcomes in pediatric patients with acute GVHD. Transplant Cell Ther. 2024;30(6):603.e1–603.e11. doi:10.1016/j.jtct.2024.03.022.
24. Shaffer BC, Gooptu M, DeFor TE, Maiers M, Bolaños-Meade J, Abboud R, et al. Post-transplant cyclophosphamide-based graft-versus-host disease prophylaxis attenuates disparity in outcomes between use of matched or mismatched unrelated donors. J Clin Oncol. 2024;42(28):3277–3286. doi:10.1200/JCO.24.00184.