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Epidemiological Profile of Adult Hematopoietic Stem Cell Transplantation for Malignant Diseases: Experience from a Reference Service in Urmia, Iran (2010-2024)

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Abstract

Background: Hematopoietic stem cell transplantation (HSCT) is a critical therapeutic option for patients with specific malignancies. This study aimed to elucidate the epidemiological profile of HSCT to address existing gaps in understanding regional trends and outcomes over 14 years at a single center.

Methods: This retrospective cohort study analyzed the medical records of all patients who underwent HSCT at the Bone Marrow Transplant (BMT) ward of Urmia Imam Khomeini Hospital in Iran, from December 2010 to December 2024. Comprehensive evaluations of clinical and demographic characteristics were conducted during the pre-HSCT period. Data collection focused on post-transplant clinical outcomes and complications, adhering to standardized definitions to ensure unbiased estimates.

Results: This study examined 280 HSCT patients, predominantly men (59.6%), with a mean age of 45.85 years (SD, 13.70). Autologous HSCT comprised 76.43% of cases, followed by allogeneic (21.78%) and haploidentical donor HSCT (1.79%). The primary indications were multiple myeloma (48.9%) and acute myeloid leukemia (24.3%). The median overall survival (OS) was 77 months (95% CI: 62.05–91.95), and a 5-year OS rate of 54%. The mean disease-free survival (DFS) was 86.21 months (95% CI: 74.62–97.81), with a 5-year DFS rate of 67%. The cumulative incidence of acute graft-versus-host disease (acute GVHD) was 59.2% at 100 days post-transplant (61% in allogeneic and 40% in haploidentical patients), with skin being the most affected organ (78.12%). Last, 20.2% of the mortality in the total population with available acute GVHD was attributed to having grades 3 and -4 acute GVHD.

Conclusion: These findings underscore the viability of hematopoietic stem cell transplantation in resource-limited settings, highlight areas for improvement in post-transplant care—particularly regarding severe acute GVHD—and offer valuable insights to guide clinical practice and health policy in similar regional centers.

Keywords: Hematopoietic Stem Cell Transplantation, Survival Rate, Transplantation-Related Complications, Hematologic Neoplasms, Neoplasms, Iran

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↑What is "already known" in this topic:
Hematopoietic stem cell transplantation (HSCT) is a critical therapy for malignant diseases, offering potential long-term survival. It includes autologous, allogeneic, and haploidentical types, each with distinct benefits and risks, like graft-versus-host disease (GVHD).

→What this article adds:
It highlights autologous transplants for multiple myeloma and allogeneic transplants for acute myeloid leukemia. This study demonstrates comparable HSCT long-term outcomes (such as overall survival and disease-free survival) with other nations, although these transplantations were performed with limited resources in a referral transplant hospital. It is notable to report that the incidence of severe GVHD was high that underscores the need for improved post-transplant care to further enhance patient outcomes and accessibility in underserved areas.

Introduction

Hematopoietic stem cell transplantation (HSCT) represents a critical therapeutic modality for a range of hematologic malignancies, with its application demonstrating a marked increase in recent years (1). This medical intervention entails the infusion of hematopoietic stem cells to reconstitute hematopoiesis in patients with impaired bone marrow function or compromised immune systems. HSCT can be categorized into allogeneic transplantation, utilizing donor-derived cells, and autologous transplantation, employing the patient's previously procured stem cells. This procedure is fundamental in the treatment of conditions such as leukemia, sickle cell disease, and diverse immune dysfunctions (2). Despite its importance, scholarly investigations underscore disparities in access to and outcomes after HSCT that are associated with racial and ethnic affiliations, thereby introducing further complexity to the discourse (3, 4).

The Asia-Pacific region has experienced the most substantial augmentation in the volume of HSCTs performed, with allogeneic transplants, frequently involving related donors, constituting a more prevalent modality than autologous procedures. Within the 18 constituent countries and regions, a discernible heterogeneity exists in per capita transplant rates, reflecting both the aggregate number of HSCTs conducted and the respective population sizes of these entities (5). Research conducted by the Worldwide Network for Blood and Marrow Transplantation offers valuable insights into the Eastern Mediterranean Region (EMR), with a specific emphasis on the Islamic Republic of Iran. A significant proportion of the data about bone marrow transplantation within Iran originates from prominent institutions located in Tehran, such as the Hematology-Oncology and Stem Cell Transplantation Research Center affiliated with Tehran University of Medical Sciences, particularly Shariati Hospital, a leading center in this field (6).

The inaugural bone marrow transplantation center in Iran was established in 1992 at Shariati Hospital in Tehran, Iran. Subsequent developments have been implemented to address the escalating demand for HSCT procedures (7). The contemporary landscape of bone marrow transplantation (BMT) for hematologic malignancies in Iran demonstrates significant progress and refinement within this specialized medical field. This includes advancements in regions such as Urmia, where facilities have been developed to rival the pioneering centers in Iran. Urmia, the provincial capital of West Azerbaijan in northwestern Iran, houses the Urmia Imam Khomeini Hospital, which functions as the principal center for bone marrow transplantation within the region. This hospital achieved a significant milestone by successfully performing its first transplant in December 2009. Notably, it conducted the first peripheral blood stem cell transplant in West Azerbaijan for a patient diagnosed with acute leukemia, thereby establishing Urmia as the third city in Iran to offer this critical medical service (8). following the precedents set by Tehran and Shiraz (9).

Comprehending the epidemiological characteristics of HSCT is paramount for informing public health strategies directed at enhancing access to this therapeutic intervention for underserved populations, thereby mitigating health inequities (4,10). Furthermore, the global prevalence of hematologic malignancies is on an upward trajectory, underscoring the imperative for effective treatment modalities such as HSCT. Analyzing these epidemiological trends can provide valuable insights for public health initiatives and clinical practices on a global scale (11). The present study focuses on elucidating the epidemiological profile of HSCT at the Urmia Imam Khomeini Hospital—the principal referral center in northwestern Iran—to address existing gaps in the understanding of regional trends, outcomes, and challenges associated with this procedure. Specifically, this investigation aimed to analyze patient demographics, transplant modalities (autologous, allogeneic, haploidentical), survival rates, and the incidence of complications such as graft-versus-host disease (GVHD). The overarching objective of this study is to provide data that can inform and guide equitable resource allocation and the development of policies aimed at improving HSCT accessibility and outcomes for populations residing in resource-constrained provinces.

Methods

A retrospective cohort study of patients diagnosed with hematological and nonhematological malignancies who underwent HSCT within the BMT unit of Urmia Imam Khomeini Hospital, located in Iran, was used to address the epidemiological profile and clinical outcomes of patients who underwent HSCT in this center. This medical facility functions as the principal center for the management, treatment, and provision of medical interventions for those with cancer and those requiring bone marrow transplantation. Specifically, patients at this institution receive peripheral blood stem cell transplants. The cohort included all patients who received HSCT between 2010 and 2024.

The analytical framework of this study centered on a range of pre-HSCT factors, encompassing the transplant modality (allogeneic, autologous, or haploidentical), the primary diagnoses of patients meeting HSCT eligibility criteria, and pertinent demographic attributes. The index date was operationalized as the commencement date of the transplantation procedure, with subsequent follow-up extending until December 2024. To mitigate the potential for underestimation of overall survival (OS) and disease-free survival (DFS) rates, patients with a follow-up duration of less than 6 months were excluded (14 patients).

All post-HSCT outcome data were retrospectively collected through medical health records. This encompassed longitudinal follow-up information pertaining to clinical endpoints and other HSCT-related sequelae. The primary outcomes evaluated included the cumulative incidence of acute graft-versus-host disease (acute GVHD), diagnosed based on clinical manifestations confirmed by an oncologist, with severity graded according to organ involvement

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before day 100 post-transplant, relapse of the primary malignancy, graft rejection, overall survival, and disease-free survival. Furthermore, nonrelapse mortality attributable to transplant-related complications was defined by the presence of immune complications (including acute GVHD, chronic GVHD, and graft rejection), infections (comprising sepsis, pulmonary infection, fungal infection, and hemorrhagic cystitis), organ toxicities (such as end-stage renal disease, renal failure, myocardial infarction, and renal dysfunction), graft-related issues (including poor graft function and aplasia), bleeding events secondary to HSCT-associated thrombocytopenia, GVHD, or infections, and other complications (such as ocular GVHD and other ocular manifestations).

We employed a multisource data acquisition strategy to mitigate potential inaccuracies and minimize information bias. Researchers utilized several data streams to evaluate outcomes and complications, including GVHD and its associated severity (12). Data were abstracted from patient medical health records, physician-prescribed medications documented in the electronic prescription system, and clinical symptomatology was cross-referenced with established EBMT criteria to ensure internal consistency and reliability. For cases of severe acute GVHD, inpatient records from post-transplant follow-up visits were scrutinized to enhance data accuracy. Furthermore, direct contact was made with patients to ascertain their vital status (alive or deceased). This comprehensive methodological approach facilitated a more precise evaluation of the data and reduced the incidence of errors, particularly in the context of the absence of a standardized registry system providing high-quality data for this patient population.

Statistical Analysis

Descriptive statistical methodologies were employed to characterize the demographic and clinical attributes of the patient cohort. Kaplan-Meier survival curves were generated to depict the cumulative incidence of specified outcomes. Patient survival time was operationalized as the interval from the date of HSCT until either mortality due to any HSCT-related cause or the date of the final recorded follow-up visit. Relapse of the primary disease, BMT rejection, and transplant-related complications, encompassing acute GVHD and infections, were categorized as transplant-related mortality (TRM). DFS time was calculated as the duration from the date of HSCT to disease recurrence, and DFS rates were subsequently determined. Statistical analyses were performed utilizing STATA Version 17 and Microsoft Excel 2019 software.

To evaluate the influence of grades 3 and 4 acute GVHD on mortality, mortality rates were calculated for both the severe acute GVHD cohort and the cohort without severe acute GVHD. The mortality rate for each group was determined by calculating the ratio of the number of deaths to the total number of patients within that group. To calculate the relative risk (RR) of mortality associated with severe acute GVHD, the RR was computed by dividing the mortality rate observed in the severe acute GVHD cohort by the mortality rate in the cohort without acute GVHD. Furthermore, the population attributable risk percentage (PAR%) was calculated to estimate the proportion of mortality within the total study population with available acute GVHD status that could be attributed to severe acute GVHD. The formula for PAR% is as follows:

$$PAR\% = \frac{100 \times Px \times (RR-1)}{1+Px \times (RR-1)}.$$

Where P_x represents the proportion of the study population exposed to severe acute GVHD, and RR denotes the RR of mortality associated with severe acute GVHD. Furthermore, the absolute increase in the risk of mortality attributable to severe acute GVHD was estimated by calculating the arithmetic difference between the mortality rate in the unexposed cohort and the mortality rate in the exposed cohort.

Results

Study Population and Demographic Characteristics

Our institution admitted a total of 280 HSCTs, comprising 215 autologous (76.43%), 60 allogeneic (21.43%), and 5 haploidentical transplants (1.79%). The study cohort consisted of 167 male participants (59.6%) and 113 female participants (40.4%), with a mean age of 45.85 years (SD = 13.70; age range: 15-73 years). Notably, the majority of patients (98%; n = 274) were residents of West Azerbaijan province, highlighting the center's crucial function as a regional healthcare provider (Table 1). PBSCs constituted the sole source of graft material for all transplantation procedures. Among the hematologic malignancies necessitating HSCT, Multiple Myeloma (MM) (48.9%) and Acute Myeloid Leukemia (AML) (24.3%) were the most prevalent, followed by Hodgkin Lymphoma (HL) (15%), Non-Hodgkin Lymphoma (NHL)(7.86%), Acute Lymphoblastic Leukemia (ALL) (0.71%), and chronic myelogenous leukemia (CML) (0.36%). Other indications collectively accounted for 3.2% of cases, including primary CNS lymphoma (1.4%), amyloidosis (0.7%), germ cell tumors (0.36%), and medulloblastoma (0.36%). The distribution of disease indications exhibited marked variation according to transplant modality: AML was the predominant indication among allogeneic HSCT recipients (93.3%), whereas MM constituted the primary indication for autologous procedures (62.8%). Haploidentical HSCTs were predominantly performed for the treatment of AML (80%).

Trends in HSCT Numbers and Indications Over Time

The volume of HSCTs performed at the center demonstrated an increasing trend throughout the study period, ranging from a nadir of 2 procedures in 2010 to a peak of 55 procedures in 2024 (Figure 1 and accompanying tabular data). Autologous transplantation consistently represented the predominant annual modality, accounting for 87.3% (n = 48) of all cases performed in 2024. Allogeneic transplantation exhibited sporadic growth patterns, reaching a maximum of 16 procedures in 2023, while haploidentical transplantation, introduced in 2020, remained an infrequent procedure (n = 5).

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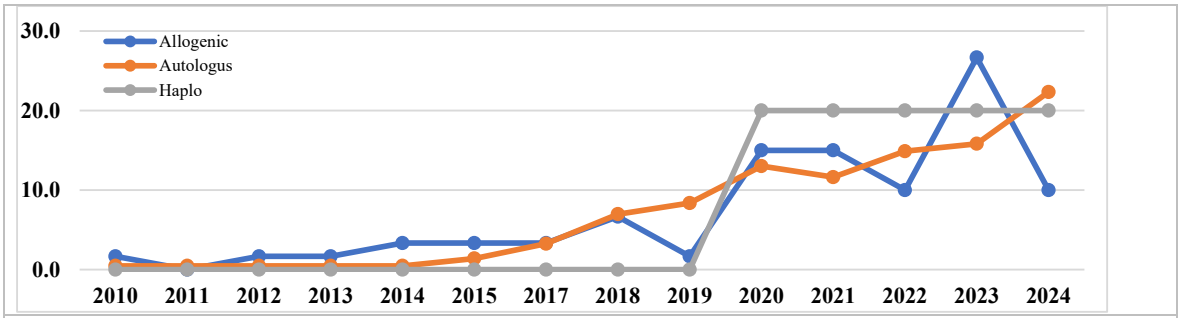
Table 1. Characteristics of HSCT Cohorts at the Urmia BMT Center (2010-2024)

Patients with HSCT		N=280	Patients' outcomes		
Autologous		214 (76.43 %)	Cumulative Incidence Acute GVHD (%)		
Allogeneic		61 (21.78 %)	Grade 1-2		17 (26.15)
Haploidentical		5 (1.79 %)	Grade 3-4		20 (30.77)
Sex	Male	167 (59.6 %)	Median OS $_{month}$ (95 % CI)		77 (62.05 – 91.95)
	Female	113 (40.4 %)			
Age at transplant		45.83 (13.62)	Mean DFS $_{month}$ (95 % CI) **		86.21(74.62 – 97.81)
Diagnosis at transplant			Survival probability (%)		OS DFS
MM		137 (48.9 %)		6 months	85 93
AML		68 (24.3%)		1 years	75 85
ALL		2 (0.7%)		3 years	64 76
HL		42 (15 %)		5 years	54 67
NHL		22 (7.9 %)	Cause of death		
Other *		9 (3.2 %)	HSCT complication		26 (30.95 %)
Chronological Number of HSCT			relapse		51 (60.71 %)
1		276 (98.57 %)	Unknown		7 (8.34%)
2		4 (1.43 %)	* CML, primary CNS lymphoma, Amyloidosis, Lymphoma, Germ Cell Tumor, Medulloblastoma		
3≤		-	** Median not calculable due to censoring patterns		
Donor sex mismatch					
	Yes	35 (53.8 %)			
		30 (46.2 %)			



HSCT type	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	N
Allogenic	1	0	2	1	2	2	-	2	4	1	9	9	6	16	6	60
Autologous	1	1	1	1	1	3	-	7	15	18	28	25	32	34	48	215
Haplo	0	0	0	0	0	0	-	0	0	0	1	1	1	1	1	5
Total	2	1	2	2	3	5	-	9	19	19	38	35	39	51	55	280

Figure 1. Trends in the Proportions of Allogeneic, Autologous, and Haploidentical Hematopoietic Stem Cell Transplants at the Urmia BMT Center (2010-2024).

Survival Outcomes

The patient cohort exhibited a median OS of 77 months (95% CI: 62.05-91.95), with no statistically significant difference observed according to sex (Figure 2; $P = 0.92$). The estimated OS rates at 6 months, 1 year, 3 years, and 5 years were 85%, 75%, 64%, and 54%, respectively, with a median follow-up duration of 22 months. Mortality was observed in 32.3% of the patient population (95% CI: 26.66-38.32), while disease relapse occurred in 18.84% (95% CI: 14.28-24.14) of the cohort.

The mean DFS duration was 86.21 months (95% CI: 74.62-97.81); the median DFS was not calculable due to censoring patterns. No statistically significant difference was observed according to sex (Figure 3; $P = 0.65$). DFS rates at 6 months, 1 year, 3 years, and 5 years were 93%, 85%, 76%, and 67%, respectively (Figure 3). In the studied population, a substantial proportion of patients remained event-free after the study, with the majority of relapses occurring towards the end of the follow-up period. These DFS rates correspond to the aforementioned OS rates of 85%, 75%, 64%, and 54% at 6 months, 1 year, 3 years, and 5 years.

Early Post-transplant Outcomes

At 100 days post-transplantation, the cumulative mortality rate was 0.08 (n = 22), with a median time to death of 25 days, yielding an estimated survival probability of 92% (95% CI: 88.5-95.5). The primary causes of mortality were relapse of the underlying malignancy (60.71%), followed by complications arising from HSCT (30.95%), with a minor proportion of cases having undetermined causes of death (8.34%). Acute GVHD was diagnosed at a

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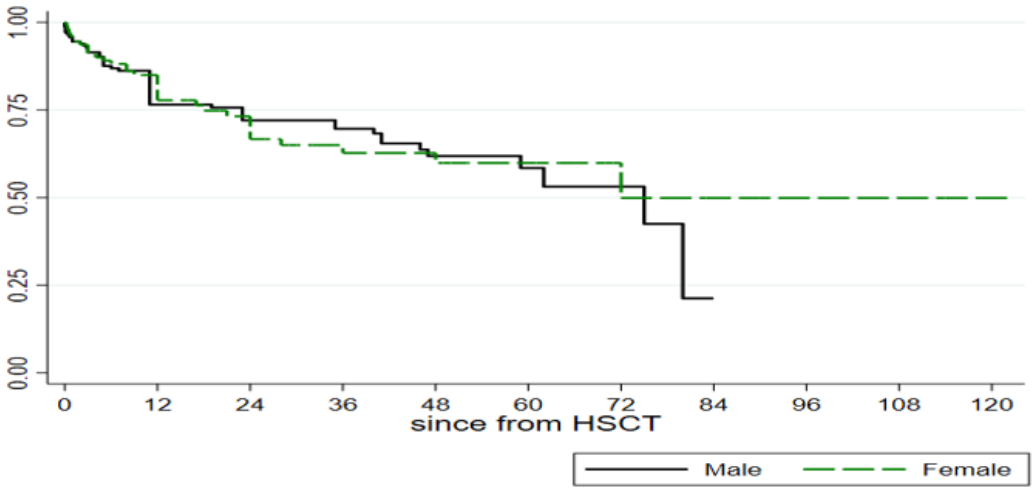

Figure 2. OS times among HSCT patients by sex at the Urmia BMT Center (2010–2024)

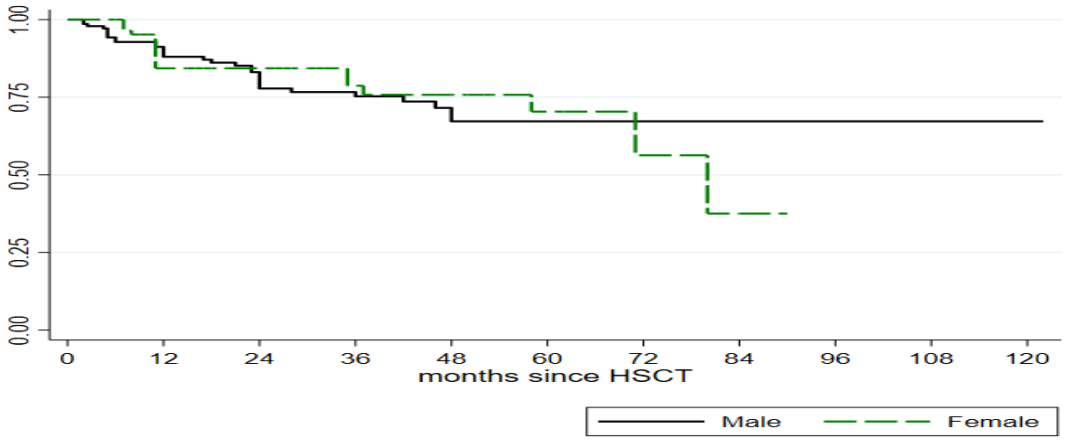

Figure 3. DFS times among HSCT patients by sex at the Urmia BMT Center (2010-2024)

median of 10 days post-transplant, with an overall incidence of 56.92% within the initial 100-day period. The cumulative incidence of acute GVHD at 100 days was 59.2%, demonstrating variation across transplant modalities: allogeneic (61%) and haploidentical (40%). Among patients diagnosed with acute GVHD, 26.15% experienced grades 1 and 2 severity, while 30.77% presented with grades 3 and 4 severity. The integumentary system was the most frequently involved organ (78.12%), followed by lower gastrointestinal manifestations (26.56%), and involvement of the upper gastrointestinal tract and liver (14.06% each). The cumulative proportion of patients surviving without the development of acute GVHD was estimated at 40.8% (SE = 0.063), indicating that less than half of the cohort remained free from this complication during the follow-up period.

Mortality Analysis in Grades 3 and 4 Acute GVHD Subgroup

The study cohort comprised 65 patients who underwent allogeneic and haploidentical HSCT. Among these, 20 patients developed grades 3 and 4 acute GVHD. In the cohort with severe acute GVHD, 17 deaths occurred, compared with 21 deaths in the cohort without severe acute GVHD. The calculated mortality rates were 85% (17 out of 20) in the severe acute GVHD group and 46.67% (21 out of 45) in the group without severe acute GVHD.

The proportion of the study population exposed to severe acute GVHD was 30.8% (20 out of 65). Application of the PAR% formula indicated that approximately 20.2% of the mortality observed in the total population with available acute GVHD status could be attributed to the presence of grades 3 and 4 acute GVHD.

Alternatively, the absolute increase in mortality risk attributable to severe acute GVHD was estimated to be 38 percentage points, representing a 38% increase in mortality risk associated with severe acute GVHD. These findings suggest a statistically significant association between severe acute GVHD and an elevated risk of mortality compared with patients who did not develop severe acute GVHD.

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Discussion

The current landscape and persistent expansion of HSCT reflect a significant augmentation in HSCT activity, particularly within low- and middle-income countries that operate under resource limitations (13). HSCT serves as a critical therapeutic intervention for patients afflicted with hematological malignancies, especially those presenting with high-risk or relapsed disease. While a clear positive trajectory exists in the adoption of HSCT procedures, the absolute number of patients undergoing this treatment exhibits regional and temporal variability. Pertinent epidemiological data illuminate the prevalence of HSCT. Within the member countries of the Asia Pacific Blood and Marrow Transplantation Group (APBMT), substantial regional disparities exist in the density of facilities offering HSCT services (14). Reports from countries within the Eastern Mediterranean and African regions, based on data spanning 2006 to 2013, indicate that a mere 12 out of 68 countries in the African Region (AFR) and Eastern Mediterranean Region (EMRO) possessed active bone marrow transplant teams. These teams reported a cumulative total of 2331 HSCTs, representing a mere 3.3% of the global volume, thus indicating the lowest regional HSCT rates relative to the eligible patient population (15).

This study delineates the epidemiological characteristics and clinical outcomes of HSCT in adult patients with hematologic and nonhematologic malignancies at Urmia, the third established transplant center in Iran, over the preceding 15-year period. The most frequent malignancies necessitating HSCT at this center were MM, HL, and AML. The 2017 Activity Survey Report from the APBMT corroborates these trends in transplant indications, identifying AML as the predominant indication for allogeneic HSCT and MM as the most common for autologous HSCT (14). Nationally, Iran has witnessed a substantial volume of HSCT procedures performed for hematological malignancies, with a discernible temporal increase in transplant numbers. Between 1991 and 2010, the pioneering transplant center in Iran executed over 3170 HSCTs, predominantly allogeneic, with AML, major thalassemia, and ALL being the most frequently treated conditions (16). Despite these advancements at the national level, comprehensive reporting from the Urmia center has been limited, underscoring the necessity for more detailed data regarding HSCT activities within this specific region. This information gap is particularly evident in APBMT reports, which predominantly feature statistical data from Tehran University of Medical Sciences, notably Shariati Hospital (14). Another bone marrow transplant center situated in northwest Iran, Imam Reza Hospital in Kermanshah, reported the successful completion of 66 bone marrow transplants between 2017 and 2019. Among these, approximately one-third were autologous transplants, with a higher representation of male patients and a median patient age range of 41 to 50 years. MM and AML were identified as the primary indications for HSCT at this institution (17).

In another HSCT center located in East Azerbaijan province, approximately 390 cases were documented between 2015 and 2023, with approximately one-third of these procedures being allogeneic transplants (18). A comparative analysis of HSCT data across various Iranian centers reveals a heterogeneous spectrum of hematological malignancies treated with this modality. Contemporary reports from bone marrow transplant centers indicate that autologous transplants constitute the most frequently performed procedure, with a higher proportion of male patients undergoing transplantation relative to female patients (7, 17). Initially, AML represented the predominant malignancy treated with transplantation in Iran (7); however, more recent data illustrate an increasing proportion of patients with MM among those receiving HSCT.

This evolving trend can be attributed to a confluence of factors, most notably the elevated prevalence of MM and leukemia within the Iranian population (19). Advancements in diagnostic modalities have enhanced the early detection of MM, thereby facilitating timely referrals for HSCT (20). A significant determinant of this pattern is the established role of autologous stem cell transplantation following high-dose chemotherapy as a cornerstone of therapeutic intervention for MM. Furthermore, in contrast to patients with other hematologic malignancies, a subset of individuals with MM may derive benefit from tandem transplantation, thus broadening their therapeutic options (21).

As previously elucidated, comprehensive data regarding the patterns and outcomes of transplantation recipients across diverse regions within Iran, particularly at bone marrow transplant centers, remains insufficiently documented, except information emanating from 2 prominent national centers. Given the escalating utilization of BMT for the treatment of malignancies and the inherent severity of these conditions, a significant imperative exists for systematic patient follow-up (1, 16). Consequently, the development of a cohesive registry system is essential, as it would serve a critical function in optimizing patient care and facilitating the timely dissemination of relevant information at the regional level (22, 23).

The present investigation observed a median OS of 77 months within the studied patient cohort. The OS probabilities at 1, 3-, and 5-year post-transplantation were 75%, 64%, and 54%, respectively. Concurrently, the DFS probabilities at these corresponding intervals were 85%, 76%, and 67%. Contemporary research has provided valuable insights into the survival rates and outcomes of HSCT recipients in Iran. For instance, a study focusing on patients with multiple myeloma reported 1-year and 5-year OS rates of 78% and 35.6%, respectively, alongside DFS rates of 57.7% at 1 year and 17% at 5 years, underscoring the challenges associated with maintaining remission after HSCT (24). Within the specific context of HL, the 3-year OS and DFS were reported as 91.8% and 77%, respectively (7). Among patients with AML, the 2-year OS rate was reported at 55%, with a relapse rate of 6% (25). Furthermore, in a separate center in Iran, AML patients who underwent allo-SCT had a 5-year OS rate of 56% and a DFS rate of 52% (26). Overall, the findings of our study suggest that patients receiving HSCT at our institution expe-

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rience comparatively favorable long-term outcomes relative to those reported in other regions within Iran.

Notably, our analysis revealed an intriguing observation wherein the median OS was shorter than the mean DFS after HSCT. Typically, OS encompasses the total duration of survival, irrespective of disease status, whereas DFS specifically measures the interval free from relapse or disease progression (27). To elucidate this apparent discrepancy, we analyzed the temporal distribution of relapses and the causes of mortality within our cohort. The mean time to relapse was 26.94 months, with a considerable proportion of relapses occurring relatively late in the post-transplantation period. Consequently, these late relapses may not immediately impact DFS, as DFS is calculated from the time of transplantation until the first documented occurrence of relapse or disease progression. However, such late relapses can ultimately compromise OS if patients succumb to their underlying disease or associated complications, thereby affecting long-term survival outcomes. This phenomenon underscores the importance of considering both DFS and OS as distinct yet complementary metrics when evaluating the efficacy of HSCT. Moreover, it highlights the necessity for sustained surveillance and tailored management strategies to address late relapses and ultimately improve overall survival rates (22).

Building upon prior observations, the present study revealed an early mortality rate of 8% among patients who underwent HSCT, with a median time to mortality of 25 days post-transplant. The reported 92% survival rate at this early stage is particularly encouraging when juxtaposed with historical data indicating substantially higher early mortality rates. It is noteworthy that approximately 60% to 80% of TRM typically occurs within the initial 100 days after transplantation (28). Our findings align with previous studies reporting an overall cumulative incidence rate of early TRM of <10% (29). Early TRM poses a significant clinical challenge, particularly during the first 100 days post-transplant, a period characterized by a heightened incidence of complications. Several factors can influence mortality rates after HSCT, including the transplant modality (autologous versus allogeneic), the patients' underlying conditions, and the development of complications such as GVHD. GVHD remains a principal contributor to mortality among HSCT recipients and exerts a considerable impact on long-term survival outcomes (30). While mortality within the first 100 days post-transplant was infrequent in our cohort, the observed discrepancy between long-term outcomes, specifically DFS and OS, may be partially attributable to early NRM. To further elucidate this, we conducted analyses of the causes of death during 2 distinct post-transplant periods: the initial 6 months and the subsequent period from 6 months to 1 year. Additional analyses focused on differentiating between relapse-related and non-relapse-related causes of death. These results indicated that 63.64% of early mortality cases were attributable to complications of HSCT rather than disease relapse, underscoring the significant impact of transplant-related complications on early mortality outcomes. Furthermore, in our cohort, the cumulative incidence of acute GVHD at 100 days post-transplant was estimated at

59.2%. Specifically, 26.15% of these cases were classified as grade 1 or 2, while 30.77% were grade 3 or 4. This finding is consistent with a prior study reporting a 29.6% incidence of acute GVHD among Iranian patients between 2007 and 2017, highlighting the significant role of acute GVHD in post-transplant events within this population (31).

Our findings demonstrate a cumulative incidence of acute GVHD of 56.92%, which is higher than the rates reported from European centers (27.9%-33%) and Asian cohorts (18.9%-40%) (32). Notably, the cumulative incidence of acute GVHD in our cohort (56.92%) exceeds rates reported in recent multinational studies (4%-17.9%), highlighting a critical disparity in outcomes that warrants further investigation into potential contributing factors such as genetic predisposition within our population, variations in immunosuppressive protocols, or other center-specific practices. Historically, studies conducted in European centers have reported acute GVHD in allogeneic HSCT recipients at rates reaching up to 33% (28). Cumulative incidences of acute GVHD at 4 months post-transplant have been reported as 27.9% and 27.6% for the first and second transplants, respectively (33). Recent research indicates a temporal decline in the cumulative incidence of acute GVHD. The incidence of grades 2 to 4 acute GVHD decreased from 47% in the period before 2000 to 24% between 2000 and 2010, and further to 16% after 2010. Similarly, the incidence of grades 3 to 4 acute GVHD decreased from 13% to 5%, and then to 4% during these same periods (34). In Asian countries, the incidence of GVHD demonstrates variability across ethnic groups. Among Japanese patients, the reported incidence of grades 2 to 4 acute GVHD is 40%, with 15.3% experiencing grades 3 to 4 acute GVHD. In contrast, Chinese patients have reported rates of 18.9% for grade 2 acute GVHD and 17.9% for grades 3 to 4 acute GVHD (35). This variability underscores the influence of donor compatibility and other clinical variables, aligning with global trends that attribute reduced GVHD incidence to advancements in human leukocyte antigen (HLA) typing precision, graft manipulation techniques, and the optimization of prophylactic regimens (36). Furthermore, mortality analysis within the acute GVHD subgroup revealed that approximately 20.2% of the total mortality in the population with available acute GVHD data could be attributed to severe acute GVHD, indicating its critical contribution to mortality in this patient cohort. The persistent burden of severe GVHD in our population may reflect region-specific challenges, necessitating more stringent HLA-matched donor selection criteria, increased utilization of alternative donor sources such as haploidentical or mismatched transplants when fully matched donors are unavailable, and the implementation of optimized prophylaxis protocols tailored to our patient population. Additionally, regional variations in gut microbiota composition, an increasingly recognized modulator of GVHD severity, warrant consideration as a potential contributing factor to the observed outcomes (37-40).

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Limitations

Several limitations warrant consideration when interpreting the findings of this investigation. First, the retrospective study design inherently introduces the potential for biases, a common methodological challenge in such analyses (41). However, the descriptive nature of this study may mitigate some concerns regarding causal inference. Second, the exclusion of patients with a follow-up duration of less than 6 months (n = 14), implemented to prevent the underestimation of overall survival, could inadvertently increase the risk of underestimating early mortality or relapse incidence. To address this concern, a review of the available follow-up data for these excluded patients (ranging from 3 to 6 months) revealed that, fortunately, none experienced disease relapse during their observed follow-up period. Third, the single-center design of this study inherently limits the generalizability of the findings to other institutions or patient populations that may exhibit differing demographic or clinical characteristics. Finally, a significant challenge encountered within the context of HSCT for hematological malignancies was the absence of detailed subtype classification for the studied malignancies, primarily attributable to the limited availability and substantial cost associated with advanced molecular and cytogenetic testing.

Conclusion

This study highlights that autologous HSCTs are mainly used for multiple myeloma, while allogeneic transplants are preferred for acute myeloid leukemia at a referral center in Northwest Iran. Despite an increase in HSCT procedures over 15 years, autologous transplants remained dominant, with few haploidentical cases, likely due to local resource constraints.

Long-term outcomes at this center are comparable to or better than national reports, reflecting progress in HSCT care. Early post-transplant mortality was low, but most deaths within 6 months were due to transplant-related complications. The higher rate of acute GVHD compared to other countries signals a need for improved management. Further research and targeted interventions are recommended to reduce non-relapse complications and improve patient outcomes.

Authors' Contributions

S.O. conceived the study, conducted data collection and statistical analyses, and wrote the initial draft of the manuscript. M.A.L. supervised the research project, critically reviewed the manuscript for intellectual content, and provided funding support. M.J. provided expertise in health information management and assisted in interpreting the results. A.J.K. interpreted the biostatistical data and contributed to the preparation of figures and tables. M.N. contributed to patient data collection and ensured the accuracy of clinical data reporting. B.E. provided overall guidance and mentorship, contributed to the discussion and conclusion sections, and approved the final manuscript. R.A. contributed to the clinical study design, provided critical input on hematological findings, and reviewed and revised the manuscript. A.A.A. assisted in interpreting clinical outcomes and contributed to discussions regarding treatment implications.

Ethical Considerations

The research obtained ethical approval from the Ethics Committee of Iran University of Medical Sciences (Approval Code: IR.IUMS.REC.1402.763). Patient information was documented and organized in medical records at Urmia Imam Khomeini Hospital. Access to this data was permitted with the authorization of the Research Deputy at Urmia University of Medical Sciences, and all findings are presented in a manner that preserves patient confidentiality. As a result, the requirement for informed consent was waived.

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Conflict of Interests

The authors declare that they have no competing interests.

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