Journal of Blood Medicine Dovepress

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Paving the Road for Haematopoietic Stem Cell Transplantation in the United Arab Emirates: A Single Centre's Experience

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Background: Despite its long-term history, haematopoietic stem cell transplantation (HSCT) still faces challenges in several countries under development and especially in the private health sector.

Objectives, Design and Methods: In this retrospective analysis, we present our experience and the results of 48 adult patients who underwent HSCT (autologous 37, allogeneic 9) at a private-sector hospital in Abu Dhabi, United Arab Emirates (UAE). The main indications were multiple myeloma and acute myeloid leukaemia in the autologous and allogeneic setting, respectively.

Results: All patients successfully engrafted, and after a median follow-up of 6 (range: 1–11) months, 42 patients are alive (36 autografted and 6 allografted). The 1-year overall survival rates were 97% and 62% for autografted and allografted patients, respectively, while 4 patients died within 100 days post-transplant from treatment-related causes (1 patient from the autografted group and 3 patients from the allografted group).

Conclusion: Our data confirm that HSCT is a feasible, safe, and effective treatment approach, offering high success rates to UAE patients with haematological malignant diseases.

Keywords: autologous stem cell transplantation, allogeneic stem cell transplantation, middle east, development, barriers, United Arab Emirates

Haematopoietic stem cell transplantation (HSCT) is considered the standard of care for patients with otherwise incurable but chemo- and immune-sensitive malignant and non-malignant disorders.[1] Despite its complexity and the need for specialized centers with contemporary and high levels of lab support along with highly experienced medical staff, HSCT is currently a routine in Western countries; however, it is still "travelling the initial steps" in several Eastern countries, including the United Arab Emirates (UAE).[2] Until recently, and despite its fast-growing economy, the UAE did not have a local health programme for patients who need HSCT. Therefore, several patients seek HSCT abroad every year, thus resulting not only in high expenditure for the procedure itself but also in suboptimal post-transplant monitoring due to the lack of centers with experienced medical staff and proper laboratory support.[3]

In February 2021, we initiated the establishment of the first comprehensive adult and paediatric HSCT unit in the UAE, in Burjeel Medical City (BMC) Hospital. Physicians and nurses, having prolonged experience in haematopoietic stem cell transplantation in international centers (Europe, USA, India), staffed the HSCT unit in BMC. Nowadays, the

Received: 24 April 2024
Accepted: 15 August 2024
Published: 4 November 2024

ultimate outcome in HSCT procedures is broadly dependent on the laboratory support. In BMC Hospital, apart from the standard laboratory tests, more specific tests like flow cytometry assays or tests of minimal residual disease (MRD) are largely provided as in-house tests. For those not provided in-house, there is a send-out service offering timely the requested results.

In October 2021, we performed the 1st autologous and, in September 2022, the 1st allogeneic HSCT in adult patients.[3]

We herein report our experience and outcomes of the first 48 adult HSCT performed during the last two years in the private sector in the UAE. This study complies with the Declaration of Helsinki, and approval from the institutional Ethics Committee has been obtained.

From October 2021 till September 2023, 39 autologous and 9 allogeneic transplants were carried out in our HSCT unit, including 27 males and 21 females with a median age of 45.5 years (range: 18–67). Multiple myeloma was the main indication for autoHSCT and acute myeloid leukaemia for alloHSCT (detailed patient characteristics are summarized in Table 1). The conditioning regimens were chosen based on the primary disease, the patient's age, and the existence of co-morbidities. Forty-four patients received myeloablative regimens (standard BEAM, high dose Melphalan, TBI-Cy, Thiotepa 10 mg/kg – Busulfan 9.6 mg/kg – Fludarabine 150 mg/m^2, or Busulfan 12.8 mg/kg – FLU 120 mg/m^2), while 4 allografted patients received a reduced intensity regimen (Thiotepa 5 mg/kg – Busulfan 6.4 mg/kg -Fludarabine 150mg/m^2 or Busulfan 9.6 mg/kg – FLU 90 mg/m^2), either due to their age or because of co-existing comorbidities. In the autologous setting, the haematopoietic stem cells (HSCs) were mobilized either with chemotherapy plus granulocyte colony stimulating factor (GCSF) or GCSF alone; plerixafor on demand was used in 10 patients. The HSCs for 9 allografted patients were collected from either full-matched siblings (n=6) or haploidentical donors (n=3) after the use of GCSF only (Table 1). All allografted patients received immunosuppressive prophylaxis for acute graft vs. host disease (aGvHD), related to the donor type and the conditioning regimen intensity (Table 1).

The statistical analysis was performed by SPSS version 22. The Kaplan–Meier method was used to calculate the differences and the survival rates.

All individuals (patients and healthy donors) successfully mobilized, and the 39 autografted patients and the 9 allografted patients received a median of 4.3 x 10^6/kg (range: 2.2–21.4) and 6 x 10^6/kg (range: 4.4–8.2) CD34+ cells, respectively. Engraftment was prompt and successful for all patients, at a median of 12 days (range: 9–33) post graft infusion (Table 1).

Among allografted patients, all but one achieved full donor chimerism within a median of 30 days (range 20–103). One patient with diffuse large B-cell lymphoma, refractory to multiple lines of treatment, received escalating doses of donor lymphocyte infusions (DLIs) because of residual disease with borderline mixed haematopoietic chimerism (94-–95% of donor origin), and the patient is currently alive with residual disease after additional chemotherapy. Clinically significant aGvHD developed in 3 patients, while chronic GvHD occurred in 2 out of 5 evaluable patients (Table 1).

After a median follow-up of 9.6 months (range: 1.2–24), 44 patients (38 autografted and 6 allografted) are alive, and 36 of them (31 autografted and 5 allografted) are assessed with undetectable disease. For the autografted patients, the projected 2-year overall survival (OS) and the 2-year progression-free survival (PFS) were 97% and 81%, respectively (Figure 1).

Importantly, all patients who were allografted with undetectable disease at the time of transplant are alive and progression-free, with a median follow-up of 5 months (range: 2–9) post-transplant. On the contrary, for patients who were allografted with active disease, the median OS and median PFS were only 2 months. Four out of 48 patients died from treatment-related causes; 1 out of 39 autografted patients died from massive central nervous system bleeding, and 3 out of 9 allografted patients died from steroid-refractory aGvHD grade IV. The projected 100- and 180-day treatment-related mortality rate for the whole group of patients is 9%.

The post-transplant outcomes at our centre, are in agreement with those reported by experienced centres in Western countries and by international registries (EBMT, CIBMTR).[1,4] It is well-documented that patients in remission or with chemo-sensitive disease have significantly better outcomes as compared with those with refractory or active disease at the time of transplant.[1,4–6] Our patients who have been transplanted in an early disease phase and especially in remission, achieved prolonged OS and PFS rates. However, 3 out of 9 (30%) of allografted patients underwent transplant late, in advanced disease phases, due to 2 major factors. The first was a delay in referral from the primary hospital that initially

Table 1 Patients' and Transplant Procedure Characteristics

	Total HSCT	Autologous HSCT	Allogeneic HSCT
Number	48	39	9
Age (med, range)	45,5 (18–67)	46 (18–67)	45(18–58)
Males	27	23	4
Females	21	16	5
Disease			
Multiple Myeloma	24	24	0
Hodgkin Lymphoma	8	8	0
Non-Hodgkin lymphoma	7	6	1
Gestational Tumor	1	1	0
Acute Myeloid leukaemia	4	0	4
Acute Lymphoblastic leukaemia	2	0	2
Myelodysplastic syndrome	1	0	1
B-Thalassemia Major	1	0	1
Conditioning regimens			
Myeloablative	43	38	5
Reduce intensity	5	1	4
Mobilization			
Chemotherapy + GCSF	17	17	0
Chemotherapy + GSCF+ Plerixafor	4	4	0
GCSF alone	21	12	9
GCSF + Plerixafor	6	6	0
Graft (Peripheral stem cell)			
CD34+ x 10^6 /kg (med, range)	4,6 (2,2–21,4)	4,3 (2,2–21,4)	6 (4,4–8,2)
Donors for alloHSCT			
Full matched siblings			6
Haploidentical			3
Engraftment day (med, range)	12 (9–33)	11 (9–17)	19 (13–33)
Days for full chimerism (for alloHSCT)			30(20–103)
GvHD prophylaxis (for allogeneic HSCT)			
CSP + sort term MTX			4
PTCy + CSP+ MMF			5
Median Follow-up (months)	9,6 (1,2–24)	9,8(1,2–24)	6 (1,9–9,8)
Acute GvHD Grade ≥II	3		3
Chronic GvHD (on 5 evaluable pts)	2		2
Alive Patients	44	38	6
Progressed/relapsed patients	8	7	1
Treatment-related mortality	4	1	3
Alive & non progressed patients	36	31	5

Abbreviations: HSCT, Haematopoietic stem cell transplantation; med, median; GCSF, granulocyte colony stimulating factor; GvHD, graft vs host disease; CSP, cyclosporin; MTX, methotrexate; PTCy, post-transplant cyclophosphamide; MMF, Mycophenolate Mofetil.

managed the patient. This delayed referral was usually related to a prolonged and largely ineffective exposure to conventional chemotherapies, which may contribute to increased disease refractoriness and organ toxicity, thus impairing the beneficial outcome of transplant. The second important factor for not performing HSCT in time was either a delay of acceptance or even multiple rejections from insurance companies, since HSCT is considered a relatively expensive treatment and is covered only by the highest insurance levels in the UAE. It is well known that the higher the insurance level, the better the treatment coverage.[7] However, now that HSCT has become the standard of care for many malignant and non-malignant haematological diseases, it can no longer be considered an "extraordinary" treatment offered only to a minority of patients.

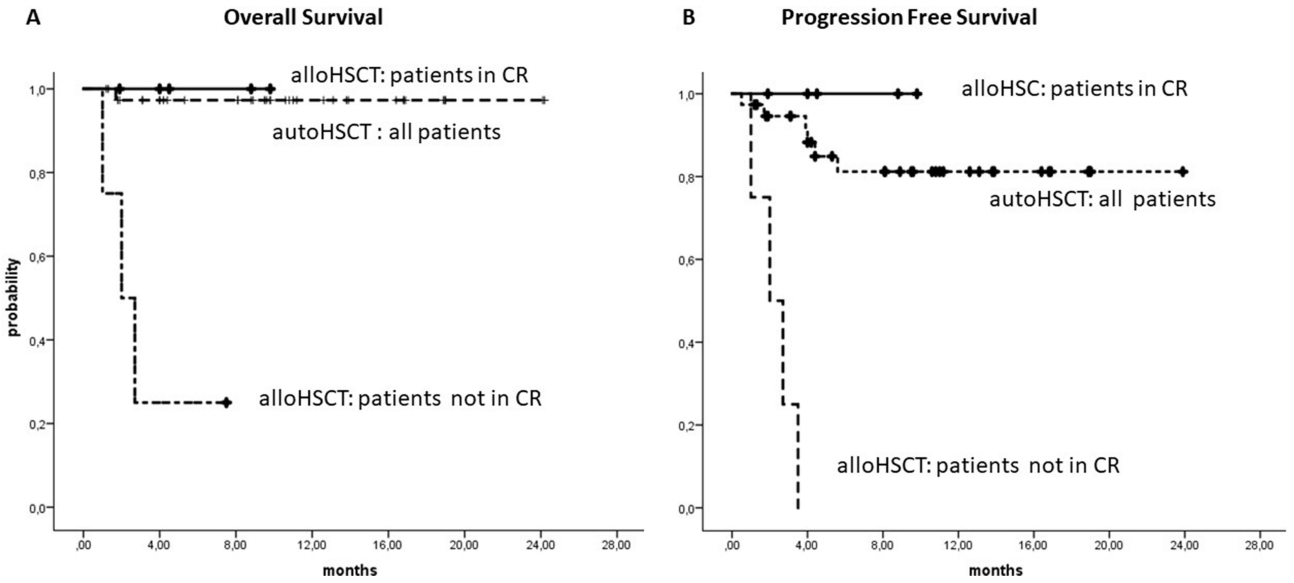

Figure 1 Survival rates for allografted and autografted patients. (**A**) Overall survival rates. (**B**) Progression-free survival rates.

In conclusion, our short-term results confirm that local implementation of HSCT, along with proper post-transplant monitoring in the private sector in the UAE, is a feasible, safe, and effective treatment approach for selected patients with haematological malignancies who have either a full-matched or a haploidentical donor. Better communication with other haemato-oncology centres in the UAE will result in the timely referral of candidate patients to the transplant centre, thus further improving the transplant outcomes. Additional efforts by health authorities and insurance companies will help to update and expand the list of the offered treatment approaches through insurance, so eventually more patients can benefit from HSCT, which is currently worldwide approved as one of the most effective treatment approaches for certain haematological malignant and non-malignant diseases.

Data Sharing Statement

The data that support the findings of this study are not openly available due to reasons of sensitivity and are available from the corresponding author upon reasonable request.

Ethics Approval

The Ethics Committee of Burjeel Medical City has approved the study (as it is already stated in the manuscript).

Consent to Participate & Publication

All patients/participants in this retrospective analysis have signed informed consent for using the clinical data for scientific purposes and for publication.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis, and interpretation. They took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; and have agreed for submission to the *Journal of Blood Medicine* and agree to be accountable for all aspects of the work.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Disclosure

The authors declare no competing financial interests.

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