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EDITORIAL

Hematopoietic cell transplants in Jordan: different indications from the US and EU

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Jordan (officially The Hashemite Kingdom of Jordan) is a small country (88,780 km E + 2; 2017 population estimate, 9.95 million) with a *per capita* GDP of US$10,074 [1, 2] and an increasing cancer incidence including haematological neoplasms [3]. Cancer care including transplants is free for Jordanian citizens but not for non-citizens whose transplant costs is paid for *out-of-pocket*, charities and rarely by the government of origin or citizenship. Numbers of Jordanians who might benefit from a haematopoietic cell transplant are increasing. There are, however, substantial barriers to meeting this need including: (1) few transplant centres; (2) few transplant specialists; (3) no volunteer donor registry with limited access to global registries; (4) high cost (US$150,000 for an allotransplant and US $100,000 for an autotransplant); (5) unavailability of some commonly used expensive transplant-related drugs; and (6) a large population of non-Jordanians with no health insurance coverage including many recent Syrian refugees. To understand the topography of transplants in Jordan we surveyed activity since 2003.

Data from three transplant centres King Hussein Cancer Center (KHCC), Jordan University Hospital (JUH) and Arab Medical center (AMC) activity from March 2003 to September 2017 were provided on data collection forms. Data from the fourth centre, the Royal Medical services (KHMC), on 100 subjects receiving transplants for immune deficiency diseases were received telephonically but are not included in this survey. Variables included numbers of transplants by year, subject ages, diagnoses and types of transplants, donor and graft. An Excel® database template was sent to data coordinators and physicians at each center and analysed at the Research Office of KHCC. Survival data were available from KHCC only. We did not audit reported data against primary medical records nor did we check hospital records to ensure consecutive reporting.

A total of 1693 transplants were reported from 2003 to 2017 including 1473 from KHCC (87%), 152 (9%) from JUH and 68 (4%) from AMC. Annual and cumulative activities are shown in Figs. 1 and 2. A total of 1321 transplant recipients (78%) were Jordanian citizens; 1006 recipients (60%) were men; 1608 transplants (95%) were in persons <50 years; 1050 (62%) were allotransplants (92% in persons <50 years); and 643 (38%), autotransplants (99% in persons <65years).

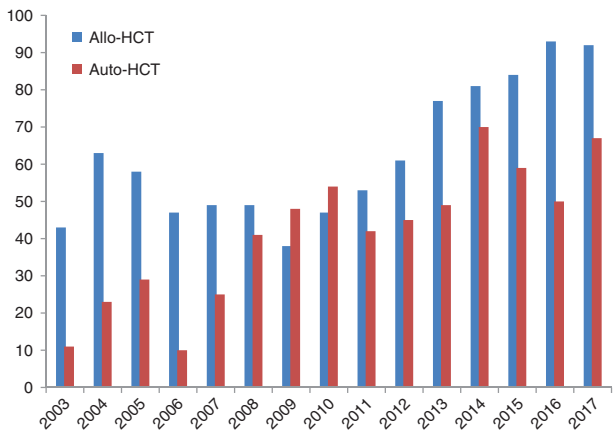

Fig. 1 Annual transplant activity (2003–2017)

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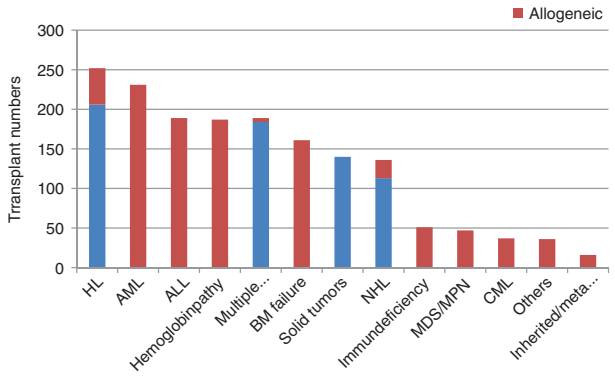

Fig. 2 Transplant activity ($N = 1693$)

The most common allotransplant indications were acute myeloid ($N = 231$; 22%) and acute lymphoblastic leukaemias ($N = 189$; 18%), haemoglobinopathies ($N = 187$; 18%) and bone marrow failure ($N = 161$; 16%; Table 1). Other indications included myelodysplastic syndrome, myeloproliferative neoplasms, chronic myeloid leukaemia, Hodgkin lymphoma, inherited and metabolic disorders and some others. The most common reasons for autotransplants included Hodgkin lymphoma ($N = 206$; 32%; Table 1), plasma cell myeloma ($N = 184$; 29%), solid cancers ($N = 140$; 21%) and non-Hodgkin lymphoma ($N = 113$; 18%). Other indications included multiple sclerosis and systemic lupus erythematous. A total of 651 allotransplant subjects (62%) received conventional high-dose pretransplant conditioning and 367 (35%) received reduced intensity conditioning. All autotransplant recipients received high-dose conditioning. HLA-matched relatives were the most common allotransplant donors ($N = 917$; 87%) followed by HLA-haplotype-matched transplants ($N = 66$; 6%), umbilical cord blood cell donors ($N = 44$; 4%) and HLA-matched unrelated donors ($N = 23$; 2%). Most of the HLA-haplotype-matched transplants were done in 2017. Most allotransplants and autotransplants ($N = 1280$; 76%) used blood cell grafts. There were 410 bone marrow allotransplants (24%) and 3 grafts of bone marrow and blood cells. Survival data are displayed in Fig. 3. The 10-year survival is 66% (95% confidence interval; 63.69%).

In conclusion, there is an increasing transplant activity in Jordan with four transplant centers performing 200–250 transplants annually. About 2/3rd are allotransplants and 1/3rd is autotransplants. The combined rate of 2–2.5/10 × 10E + 5 population is like other Arab countries in the Middle East but about fivefold lower than the EU and US [4–9]. Adjusting for the high proportion of allotransplants to autotransplants the respective rates are about three to tenfold lower than the US and EU. The distribution between allotransplants and autotransplants in Jordan is like neighbouring Arab countries. Although some aspects of transplant indications in Jordan are like those reported in the US and EU, there are important quantitative differences. For example, there was a greater proportion of allotransplants for Hodgkin than non-Hodgkin lymphomas. These data are like those reported by the Eastern Mediterranean Bone Marrow Transplant Group (EMBMT) but different than those reported by the Center for Blood and Marrow Research (CIBMTR) [10].

Table 1 Transplant indications

	Allotransplant (1050)	Autotransplant (643)
AML	231 (22%)	–
ALL	189 (18%)	–
MDS + MPN	47 (5%)	–
CML	37 (4%)	–
Hodgkin	46 (5%)	206 (32%)
PCM	5 (0.5%)	184 (29%)
NHL	23 (2%)	113 (18%)
Solid cancer[a]	–	140 (21%)
Hemoglobinopathy	187 (18%)	–
Bone marrow failure[b]	161 (16%)	–
Immune deficiency[c]	51 (5%)	–
Other inherited/ metabolic	16 (2%)	–
Other[d]	36 (3.5%)	–

AML acute myeloid leukaemia; *ALL* acute lymphoblastic leukaemia; *MDS* myelodysplastic syndrome; *MPN* myeloproliferative neoplasm; *CML* chronic myeloid leukaemia; *PCM* plasma cell myeloma; *NHL* non-Hodgkin lymphoma

[a]Solid cancers included neuroblastoma ($N = 88$), germ cell tumours ($N = 19$), Ewing sarcoma and peripheral neuro-endocrine tumours ($N = 11$), medulloblastoma ($N = 8$), Wilm tumour ($N = 5$), retinoblastoma ($N = 3$); renal cell carcinoma ($N = 3$); meningeal and synovial cell sarcomas ($N = 2$) and choroid plexus carcinoma ($N = 1$)

[b]Aplastic anaemia, Fanconi anaemia and sickle cell anaemia

[c]Does not include 100 transplants reported telephonically

[d]Includes pure red cell aplasia ($N = 6$), congenital amegakaryocytic thrombocytopenia ($N = 6$), chronic granulomatous disease ($N = 2$); osteopetrosis ($N = 2$); haemophagocytic lympho-histiocytosis ($N = 2$)

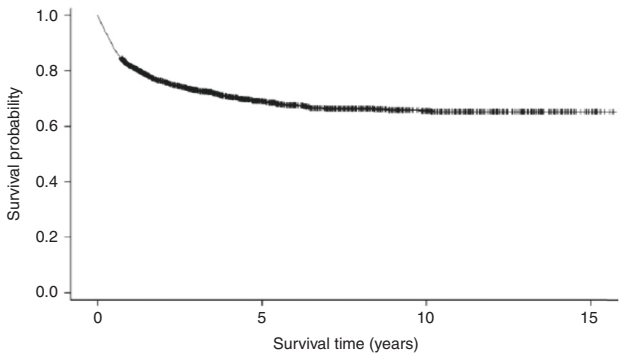

Fig. 3 Survival transplants 2003–2017 ($N = 1473$)

There was a greater proportion of allotransplants for haemoglobinopathies probably because of the increased incidence in the Middle East including Jordan. If we include the 100 transplants for immune deficiency reported telephonically the proportion of such transplants is 13%, much higher than in the US and EU (6%). Most recipients were referred from neighbouring Arab countries [10]. There were also differences in autotransplant indications with twice as many for Hodgkin versus non-Hodgkin lymphomas. twenty-one percent of autotransplants were for solid cancers (mainly neuroblastoma and germ cell cancers) compared with 5–7% of autotransplants for solid cancers in the US and EU [9, 10]. Most of these differences do not reflect different disease incidences. Although the incidence of haemoglobinopathies is higher in Jordan than the US and EU, the incidence of immune deficiency disorders is similar as are ratios of lymphomas and plasma cell myeloma to solid cancers [3]. Consequently, these discordances likely reflect physician preferences and perhaps access to transplants [9, 10].

Donors and graft types were like in the US and EU, except for very few HLA-matched unrelated donor transplants because of limited access to global volunteer donor registries and cost. There were also fewer HLA-haplotype-matched related transplants because of delayed technology diffusion into Jordan. Despite diverse challenges to expanding transplant activity in Jordan, numbers of allotransplants and autotransplants are increasing and we are optimistic about the future.

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Compliance with ethical standards

Conflict of interest RPG is a part-time employee of Celgene Corp.

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