Bone Marrow Transplantation (2017) **52,** 120–125
© 2017 Macmillan Publishers Limited, part of Springer Nature. All rights reserved 0268-3369/17
www.nature.com/bmt

ORIGINAL ARTICLE

First report of pediatric hematopoietic stem cell transplantation activities in the eastern mediterranean region from 1984 to 2011: on behalf of the pediatric cancer working committee of the eastern mediterranean blood and marrow transplantation group

AA Hussein[1], AA Hamidieh[2], A Elhaddad[3], M Ramzi[4], TB Othman[5], F Hussain[6], D Dennison[7], P Ahmed[8], M Abboud[9], A Al-Ahmari[6], A Wahadneh[10], J Fathy[3], M-A Bekadja[11], S Al-Kindi[7], S Benchekroun[12], A Ibrahim[13], M Behfar[2], M Samra[3], S Ladeb[5], S Adil[14], H El-Solh[6], M Ayas[6], M Aljurf[6], A Ghavamzadeh[2], A Al-Seraihy[6] and Pediatric Cancer Working Committee of the Eastern Mediterranean Blood and Marrow Transplantation (EMBMT) Group

To describe the hematopoietic stem cell transplantation (HSCT) activities for children in the Eastern Mediterranean (EM) region, data on transplants performed for children less than 18 years of age between 1984 and 2011 in eight EM countries (Egypt, Iran, Jordan, Lebanon, Oman, Pakistan, Saudi Arabia and Tunisia) were collected. A total of 5187 transplants were performed, of which 4513 (87%) were allogeneic and 674 (13%) were autologous. Overall, the indications for transplantation were malignant diseases in 1736 (38.5%) and non-malignant in 2777 (61.5%) patients. A myeloablative conditioning regimen was used in 88% of the allografts. Bone marrow (BM) was the most frequent source of stem cells (56.2%), although an increasing use of PBSC was observed in the last decade. The stem cell source of autologous HSCT has shifted over time from BM to PBSC, and 80.9% of autologous HSCTs were from PBSCs. The donors for allogeneic transplants were matched-related in 94.5% of the cases, and unrelated transplants, mainly cord blood (99%) in 239 (5.5%) cases. This is the first report to describe the pediatric HSCT activities in EM countries. Non-malignant disorders are the main indication for allogeneic transplantation. Frequency of alternate donor transplantation is low.

Bone Marrow Transplantation (2017) **52,** 120–125; doi:10.1038/bmt.2016.209; published online 12 September 2016

INTRODUCTION

Hematopoietic stem cell transplantation (HSCT) is a well-established therapeutic intervention for various congenital and acquired disorders of the hematopoietic system including a wide range of malignant and non-malignant disorders.[1] More than five decades have passed since the first report on the use of HSCT in children, and since that time there has been considerable progress and success of HSCT in a large variety of pediatric conditions as a result of better supportive care, refined conditioning regimens and expansion of donor stem cell sources.[2–4]

Most published reports have analyzed data obtained through combined information on both adult and pediatric patients. There are only a few large-scale studies that described the HSCT activities and strategies used in children.[5–11] Most of these published studies described the status and outcome of HSCT in developed countries and were based on data collected through regional and international registries such as: Center for International Blood and Marrow Transplant Research, European Society for Blood and Marrow Transplantation, Worldwide Network for Blood & Marrow Transplantation and the Asia-Pacific Blood and Marrow Transplantation Group.

However, reports from developing countries, particularly the Eastern Mediterranean (EM) WHO region countries, have remained scant. The younger median age of HSCT recipients, predominance of inherited diseases, relative paucity of resources and experience, and variable socioeconomic challenges are unique to this part of the world.

The Eastern Mediterranean Bone Marrow Transplantation Group (EMBMT) was established in 2007 after a number of meetings between transplant teams from the EM region, with the aim of sharing experience, initiation of collaborative trials and the establishment of common strategies for transplantation, taking into consideration the specific issues and peculiarities relevant to the region.[12–14] The EMBMT pediatric cancer working committee was established in 2009. In this study we report on HSCT activities for children in the EM region.

[1]Bone Marrow and Stem Cell Transplantation Program, King Hussein Cancer Center, Amman, Jordan; [2]Hematology, Oncology and SCT Research Center, Tehran University of Medical Sciences, Tehran, Islamic Republic of Iran; [3]National Cancer Institute, Cairo University, Cairo, Egypt; [4]Shiraz University of Medical Science, Shiraz, Islamic Republic of Iran; [5]Center National de Greffe de Moelle Osseuse de Tunis, Tunis, Tunisia; [6]King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia; [7]Sultan Qaboos University Hospital, Muscat, Oman; [8]Armed Forces Bone Marrow Transplant Center, Rawalpindi, Pakistan; [9]American University Beirut Medical Center, Beirut, Lebanon; [10]Queen Rania Al-Abdullah Children Hospital-King Hussein Medical Center, Amman, Jordan; [11]Oran University-1st November Hospital, Oran, Algeria; [12]Service d'Hematologie et Oncologie Pediatrique, Casablanca, Morocco; [13]Makassed General Hospital, Beirut, Lebanon and [14]Aga Khan University Hospital, Karachi, Pakistan. Correspondence: Dr AA Hussein, Bone Marrow and Stem Cell Transplantation, King Hussein Cancer Center, Queen Rania Al Abdullah Street, PO Box 1269, Amman 11941, Jordan.
E-mail: ayadahmedhussein@gmail.com
Received 6 July 2015; revised 2 July 2016; accepted 11 July 2016; published online 12 September 2016

MATERIALS AND METHODS

Data collection

The data on HSCTs for pediatric patients (less than 18 years of age at the time of transplant) performed between 1984 and 2011 in eight EM region countries (Egypt, Iran, Jordan, Lebanon, Oman, Pakistan, Saudi Arabia and Tunisia) were collected using allogeneic and autologous transplant survey sheets. The data collected were as follows: primary disease categories, indication of transplant, donor type, stem cell source, intensity of conditioning regimen (myeloablative versus reduced intensity) as previously defined[15] and year of transplantation. The corresponding author and the central EMBMT office contacted the major transplant centers in each country reporting to EMBMT. The survey sheets were sent to programs with consistent annual performance of $\geqslant 5$ cases per year for at least 3 years. Data were then collected and analyzed. The information regarding population and gross national income per capita was obtained from WHO-EMRO office website (http://www.who.int/about/regions/emro/en/index.html).

HSCT team density was calculated as the number of HSCT teams per 10 million population in each country.[14] The HSCT rate per 10 million population was also calculated. The list of the participating centers is shown in the Appendix.

Statistical analysis

Descriptive statistics was performed on demographic data showing counts and percentages for categorical data. A significance criterion of $P < 0.05$ was used in the analysis. Analysis was performed using SAS version 9.1 (SAS Institute Inc., Cary, NC, USA).

RESULTS

Number of transplants

A total of 5187 transplants were performed between 1984 and 2011, of which 4513 were allogeneic (87%) and 674 were autologous (13%). The number of participating transplant teams, the availability of pediatric BMT program in each country, the reported numbers of HSCTs, team density, number of HSCT per 10 million populations and information on population are shown in Table 1.

Saudi Arabia was the first country to perform HSCT (1984), followed by Lebanon (1988), Iran (1991), Oman (1995), Egypt (1997), Tunisia (1998), Pakistan (2001) and Jordan (2003). The largest number of transplants were performed in Saudi Arabia, with a total of 1977 transplants (38.2%), followed by Iran ($n = 1197$, 23.1%), Egypt ($n = 811$, 15.6%), Jordan ($n = 361$, 7%), Pakistan ($n = 325$, 6.2%), Tunisia ($n = 249$, 4.8%), Oman ($n = 162$, 3.1%) and Lebanon ($n = 105$, 2%). The highest rate of pediatric HSCT per 10 million population was reported in Saudi Arabia (820.33), followed by Oman (648), Jordan (633.33), Lebanon (262.5), Tunisia (207.5), Iran (166.25), Egypt (109.44) and Pakistan (19.23).

Team density

The gross national income per capita-based WHO income in the EM region is shown in Table 1. Most of the countries with pediatric transplant services are in the upper middle-income category, except Saudi Arabia and Oman, which are in the high-income group and Pakistan in the lower middle-income category. It is evident that there is a low-HSCT team density in most of the EM region countries. Moreover, many of high-income countries in the EM region are lacking pediatric HSCT services.

Indication for HSCT

Allogeneic HSCT. Overall, there was a significantly higher number of transplants performed for patients with non-malignant diseases ($n = 2777$, 61.5%) compared with malignant diseases ($n = 1736$, 38.5%). However, for specific disease category indication, leukemia was the main disease indication for allogeneic HSCT ($n = 1690$, 37.5%), followed by hemoglobinopathies ($n = 1081$, 24%), bone marrow failure (BMF; $n = 952$, 21%), primary immunodeficiency (PID; $n = 599$, 13.3%), inherited metabolic disease ($n = 132$, 2.9%), lymphoma ($n = 44$, 1%) and solid tumor ($n = 2$; Figure 1a).

Among patients with leukemia, AML in first CR was more common ($n = 492$, 29.1%), followed by ALL beyond CR1 ($n = 354$, 21%), ALL CR1 ($n = 328$, 19.4%), AML beyond CR1 ($n = 191$, 11.3%), CML in the first chronic phase (CP1; $n = 158$, 9.4%), myelodysplastic syndrome (MDS; $n = 78$, 4.6%) and myeloproliferative disorders, including juvenile myelomonocytic leukemia ($n = 75$,4.4%) and CML beyond CP1 ($n = 14$, 0.8%).

Table 1. Pediatric HSCT activities and related logistics indices in the EM region

Countries	*Population in millions*	*GNI per Capita US$ (WHO income category)*	*Total pediatric HSCT performed in major centers*	*Teams performing HSCT*	*HSCT team density*	*HSCT/10 million population*
Saudi Arabia	24.175	14 740	1977	1	0.42	820.33
Iran	70.270	8050	1197	1	0.14	166.25
Egypt	74.166	4440	811	1	0.13	109.44
Pakistan	160.943	2350	325	2	0.12	19.23
Tunisia	10.215	7900	249	1	0.98	207.50
Jordan	5.729	5280	361	2	3.51	633.33
Oman	2.546	1468	162	1	3.93	648.00
Lebanon	4.055	5740	105	2	4.94	262.50
Morocco	30.853	4360	NA	NA	NA	NA
Afghanistan	26.088	$\geqslant$1000	NA	NA	NA	NA
Bahrain	0.739	15 110	NA	NA	NA	NA
Djibouti	0.819	2540	NA	NA	NA	NA
Iraq	28.506	$\geqslant$3600	NA	NA	NA	NA
Kuwait	2.779	23 080	NA	NA	NA	NA
Libya	6.039	$\geqslant$12 300	NA	NA	NA	NA
Qatar	0.821	$\geqslant$80 900	NA	NA	NA	NA
Somalia	8.445	$\geqslant$600	NA	NA	NA	NA
Sudan	37.707	2160	NA	NA	NA	NA
Syria	19.408	3930	NA	NA	NA	NA
United Arab	4.248	22 630	NA	NA	NA	NA
Emirates Yemen	21.732	920	NA	NA	NA	NA

Abbreviations: EM = Eastern Mediterranean; GNI = gross national income; HSCT = hematopoietic stem cell transplantation; NA = not available.

© 2017 Macmillan Publishers Limited, part of Springer Nature.

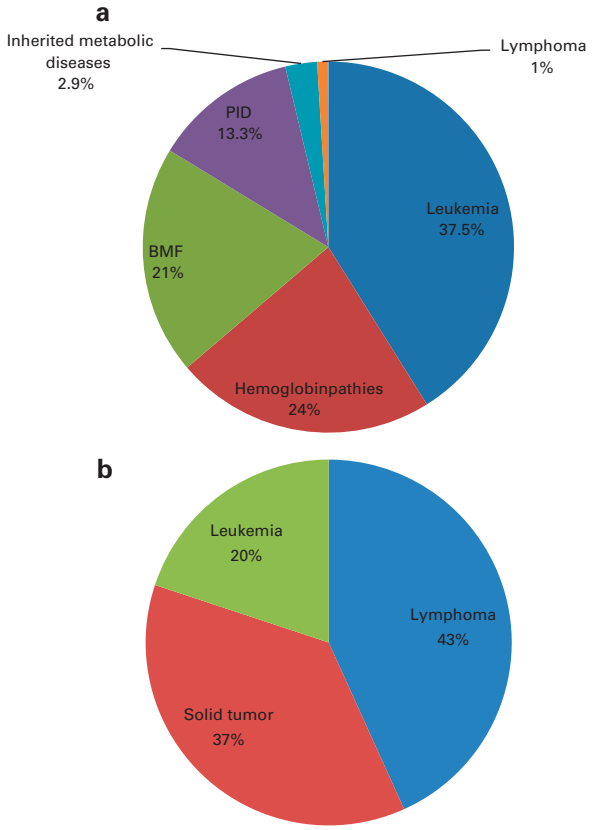

Figure 1. Relative proportions of disease indications for pediatric HSCT in the EM region from 1984 to 2011. (**a**) Allogeneic. (**b**) Autologous.

Forty-four patients received allogeneic HSCT for lymphoma, mainly non-Hodgkin's lymphoma (NHL, $n=31$), and only two patients received allogeneic HSCT for solid tumors (neuroblastoma and Ewing sarcoma).

For the non-malignant disorders, hemoglobinopathy was the most common indication ($n=1081$, 39%), mainly thalassemia ($n=1033$, 95.6%) followed by sickle cell disease ($n=32$, 4.4%). The second most common indication was BMF ($n=952$, 34.3%), mainly idiopathic aplastic anemia ($n=593$, 62.3%), followed by Fanconi anemia ($n=294$, 30.9%) and other hereditary BMF disorders ($n=61$, 6.8%). The third most common indication was PID ($n=599$, 21.6%), SCID($n=221$), followed by undefined PID ($n=214$), hemophagocytic lymphohistiocytosis-related disorder ($n=93$), leukocyte adhesion defect ($n=44$) and Wiskott–Aldrich syndrome ($n=27$). The fourth indication was inherited metabolic diseases ($n=132$, 4.8%), including 55 transplants for osteopetrosis.

Autologous HSCT. A total of 674 patients underwent autologous HSCT, with lymphoma being the main indication with 291 transplants (43.2%), followed by other solid tumors ($n=248$, 36.8%) and leukemia ($n=134$, 19.9%; Figure 1b).

Conditioning regimens

A total of 3972 patients (88%) received conventional myeloablative conditioning and 471 (10.5%) received reduced-intensity conditioning (RIC), whereas 70 patients with PID (1.5%) received no conditioning. There was significant increase in the use of RIC in the last decade (Figure 2).

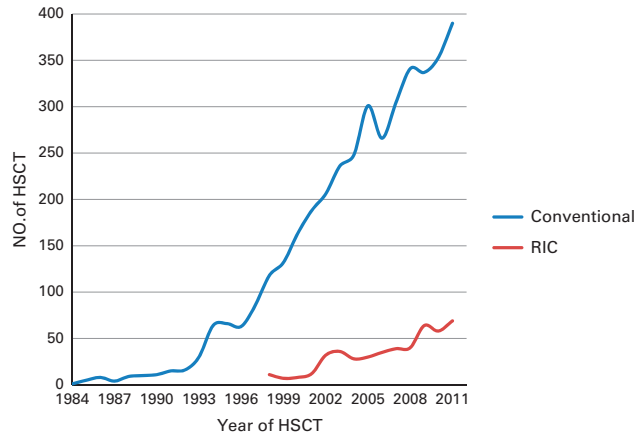

Figure 2. Trends in the use of conventional and RIC for pediatric allogeneic HSCT in the EM region from 1984 to 2011.

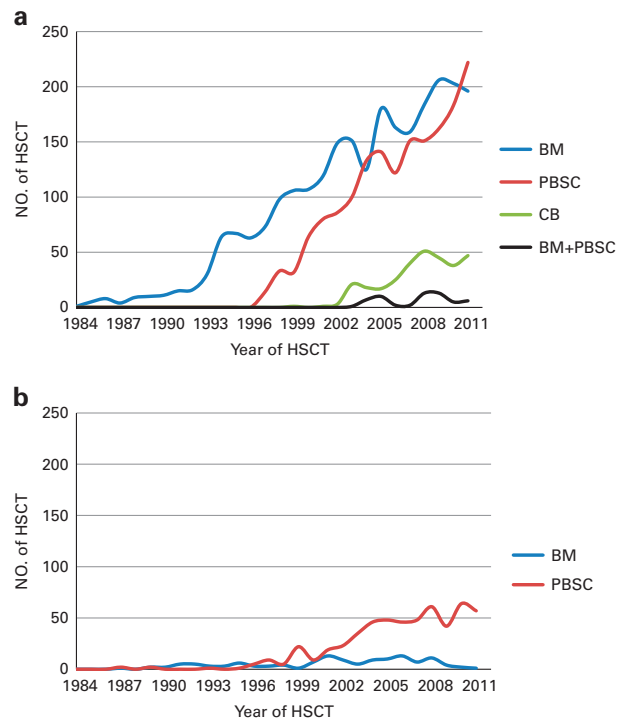

Figure 3. Trends in the use of stem cell source for pediatric HSCT in the EM region from 1984 to 2011. (**a**) Allogeneic. (**b**) Autologous.

Related versus unrelated donors

A total of 4263 patients (94.7%) received matched related allogeneic HSCT, including 22 from related cord blood (CB), whereas 239 (5.3%) patients received unrelated transplants, including 237 CB (99% of unrelated transplants) and 2 matched unrelated donor (MUD) transplants. The first unrelated CB transplant was performed in 2003. The majority of unrelated transplants were performed in Saudi Arabia (195 CB, no MUD), followed by Iran (25 CB and one MUD), Jordan (16 CB and one MUD) and Oman (one CB). Pakistan, Tunisia, Lebanon and Egypt did not report any unrelated transplants.

Stem cell source

A total of 2519 patients (55.8%) received matched related allogeneic bone marrow (BM), whereas 1676 (37.1%) received

© 2017 Macmillan Publishers Limited, part of Springer Nature.

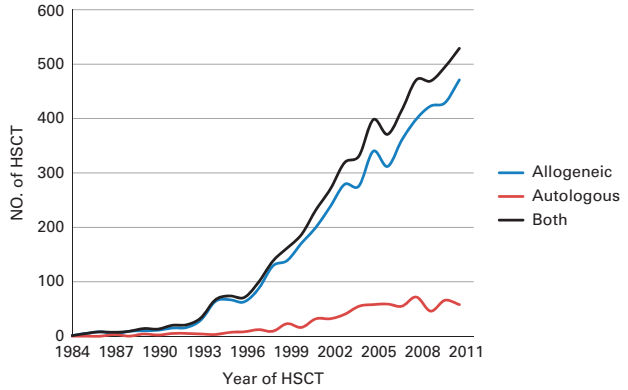

Figure 4. Trend of pediatric HSCT (allogeneic, autologous and total) in the EM region from 1984 to 2011.

PBSCs, 59 (1.3%) BM and PBSC, and 259 (5.8%) received CB transplants (22 related and 237 unrelated; Figure 3a). For the autologous group, 545 patients (80.9 %) received PBSC and 129 (19.1%) received BM as the stem cell source (Figure 3b), with a significant increase in the use of PBSC in the last decade ($P < 0.0001$).

Trend of pediatric HSCTs over years

There was a significant increase in the number of HSCT over time, starting with 132 transplants in the first decade (1984–1993), to almost 10-fold increase in the following 9 years (1994–2001) with reported 1300 transplants, and another almost 29-fold increase in the next 9 years (2003–2011) with 3755 transplants were performed (Figure 4). A trend of disease-specific indications over years was also observed, with a significant incremental rise in the number of allogeneic HSCT for leukemia, BMF, hemoglobinopathies and PID (Figure 5a), and autologous HSCT for solid tumor and lymphoma (Figure 5b).

DISCUSSION

This is the first report to describe HSCT activities for children in the EM region. The history of pediatric HSCT in the EM countries started in 1984 with matched related HSCT for a child with aplastic anemia (AA). This report analyzed data on 5187 transplants performed over almost three decades.

Between 1985 and 2011, significant progress was made in the field of pediatric HSCT in the EM region. There was a significant increase in the number of HSCTs performed for malignant and non-malignant diseases, with some differences in donor selection and disease indications among countries.

The pediatric population constitutes ~20% of the entire population in the western countries. However, in most of the EM and developing countries children represent much higher proportion of the population.[11] In addition, higher consanguinity rates and inter-related marriages lead to higher prevalence of genetic disorders, such as the hemoglobinopathies, PID, BMF and other hereditary disorders that can be cured with HSCT.[11]

Not all EM countries have comprehensive medical services to manage children with various malignant and non-malignant disorders. Accordingly, the group of patients who are in need for HSCT is heterogeneous and they often suffer from significant comorbidities upon referral to transplant services.

In several EM region countries, few or no HSCT services are available because of limited financial resources, lack of experienced medical team and inadequate governmental support.[13]

The majority of allogeneic transplants in the EM region are from matched related donors. This is not surprising as approximately

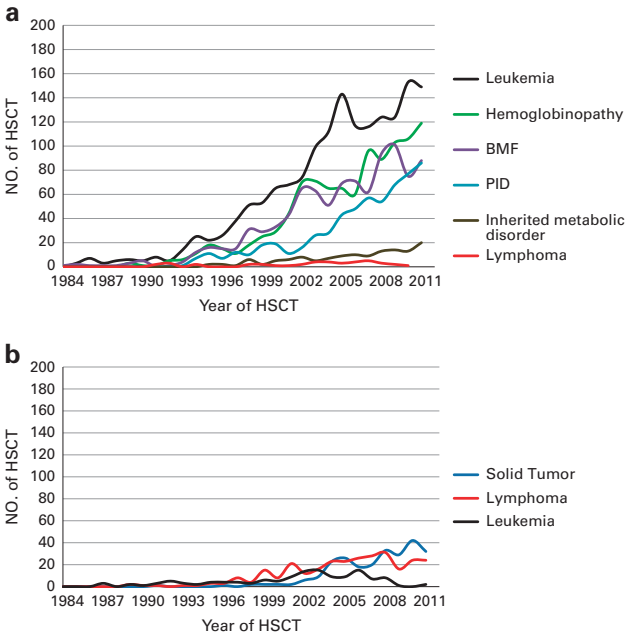

Figure 5. Trends of disease indications for pediatric HSCT in the EM region from 1984 to 2011. (**a**) Allogeneic. (**b**) Autologous.

two-thirds of children who need HSCT can find suitable sibling and other related HLA-matched donors[16–19] as a result of large families and the higher rate of consanguineous marriages.[20] It is much higher than the reported likelihood of finding matched related donors in western countries.[21,22] It is expected that the need of HSCT for children with various malignant and non-malignant diseases will continue to increase in the future. Health-care providers in the EM region will face this important demand, and they should initiate real actions to establish pediatric HSCT services. In addition, there is a growing need to establish HSCT databases and registries in the EM region, which will help in identifying the trend and outcome of HSCT.[23] The pediatric HSCT team density is low in most of the EM countries, and is still lower than other countries and regions (such as Europe).[24]

The number of transplants performed for non-malignant disorders in the EM region is higher than that for malignant diseases, which is opposite to what is reported in western countries.[24]

The most common indication for HSCT in patients with non-malignant disorders in the EM region was thalassemia major. The survival and quality of life of patients with thalassemia major with supportive therapy in developed countries is much superior than those living in developing countries.[25–28]

HSCT from HLA-matched family donor has significantly improved the prognosis of patients with thalassemia major. There are growing reports about good outcomes of HSCT for patients with thalassemia in the EM countries.[26,29,30] A significant percentage of patients with thalassemia major in the EM region suffer from iron overload, and some of them acquired hepatitis B or C infection from blood transfusions. The use of RIC–HSCT in those patients seems to be promising.[26]

We also have unique challenges in our area related to delay in the diagnosis and referral for HSCT for patients with PID, which can adversely affect the transplant outcomes.[31] Efforts to implement newborn screening might result in early diagnosis and referral to HSCT.

Data and practices of HSCT for children with BMF disorders in the EM region represent one of the largest experiences worldwide,[29,32] and can be used as resources for more research and studies in the future.

© 2017 Macmillan Publishers Limited, part of Springer Nature.

The EM region has a similar trend to western and eastern European countries with regard to an increase in the use of PBSC as the stem cell source for autologous HSCT.[8,9]

The use of PBSC as the stem cell source for matched related pediatric HSCT has grown over the last decade in the EM countries. This preference might have contributed to faster engraftment and shorter duration of hospitalization, and therefore is more convenient for donors and physicians. In addition, increasing use of PBSC with RIC for patients with non-malignant disorders might be a contributing factor.[26]

The HSCT practice in the EM region countries is heterogenous, with 18% of the centers performing pediatric transplants only, 35% performing adult transplants only and 47% performing both adult and pediatric transplants.[12] This might be related to the growing transplant experience and paucity of specialized pediatric transplant teams in the EM countries.

There is consistency in many of the pretransplant assessment measures and supportive care practice in most of the adult and pediatric EMBMT teams.[12] In primary diseases, indication and type of HSCT are different between adult and pediatric transplant services.

Because of limited resources and high cost, the use of alternative donors is very limited in the EM region. In addition, the infrastructure needed for unrelated HSCT such as CB banks, donor registries and regulations for unrelated stem cell donations is still underdeveloped and sparely distributed in the EM countries.[19] Developing haplo-identical transplant protocols using post-transplantation cyclophosphamide is likely to facilitate the performance of HSCT for patients with no related family donor.

In conclusion, this is the first report to describe the pediatric HSCT activities in EM counties. There is an increase in the number of HSCT for children in the past two decades. Non-malignant disorders are the main indications for allogeneic transplantation. Performance of alternate donor transplantation remains limited, and the majority of the procedures used CB as the alternate donor stem cell source. Building a regional unrelated registry and CB banks might improve donor availability. Efforts are underway to establish an outcome registry in the EM region.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ACKNOWLEDGEMENTS

We acknowledge and thank all medical staff of the participating teams and their data managers who collected and forwarded their data to the corresponding author and EMBMT central office.

REFERENCES

1 Copelan EA. Hematopoietic stem-cell transplantation. *N Engl J Med* 2006; **354**: 1813–1826.
2 Thomas ED, Lochte HL Jr, Lu WC, Ferrebee JW. Intravenous infusion of bone marrow in patients receiving radiation and chemotherapy. *N Engl J Med* 1957; **257**: 491–496.
3 Thomas ED, Blume KG. Historical markers in the development of allogeneic hematopoietic cell transplantation. *Biol Blood Marrow Transplant* 1999; **5**: 341–346.
4 Cairo M, Heslop H. Pediatric blood and marrow transplantation: state of the science. *Bone Marrow Transplant* 2008; **41**: 97.
5 Peters C, Minkov M, Gadner H, Klingebiel T, Vossen J, Locatelli F *et al.* European Group for Blood and Marrow Transplantation (EBMT) Working Party Paediatric Diseases; International BFM Study Group--Subcommittee Bone Marrow Transplantation (IBFM-SG). Statement of current majority practices in graft-versus-host disease prophylaxis and treatment in children. *Bone Marrow Transplant* 2000; **26**: 405–411.
6 Peters C, Ladenstein R, Minkov M, Pötschger U, Gadner H, Cornish J *et al.* Transplantation activities and treatment strategies in paediatric stem cell transplantation centres: a report from the EBMT Working Party on Paediatric Diseases. European Group for Blood and Marrow Transplantation. *Bone Marrow Transplant* 1998; **22**: 431–437.
7 Miano M, Labopin M, Hartmann O, Angelucci E, Cornish J, Gluckman E *et al.* Haematopoietic stem cell transplantation trends in children over the last three decades: a survey by the paediatric diseases working party of the European Group for Blood and Marrow Transplantation. *Bone Marrow Transplant* 2007; **39**: 89–99.
8 Miano M, Cancedda R, Hartmann O, Cornish J, Locatelli F, Egeler R *et al.* Survey on haematopoietic stem cell transplantation for children in Europe. *Bone Marrow Transplant* 2005; **35**: S3–S8.
9 Wachowiak J, Labopin M, Miano M, Chybicka A, Stary J, Sterba J *et al.* Haematopoietic stem cell transplantation in children in eastern European countries 1985–2004: development, recent activity and role of the EBMT/ESH Outreach Programme. *Bone Marrow Transplant* 2008; **41**: S112–S117.
10 Moore AS, Shaw PJ, Hallahan AR, Carter TL, Kilo T, Nivison-Smith I *et al.* Haemopoietic stem cell transplantation for children in Australia and New Zealand, 1998-2006: a report on behalf of the Australasian Bone Marrow Transplant Recipient Registry and the Australian and New Zealand Children's Haematology Oncology Group. *Med J Australia* 2009; **190**: 121.
11 Passweg J, Baldomero H, Peters C, Gaspar H, Cesaro S, Dreger P *et al.* Hematopoietic SCT in Europe: data and trends in 2012 with special consideration of pediatric transplantation. *Bone Marrow Transplant* 2014; **49**: 744–750.
12 Rasheed W, Ghavamzadeh A, Hamladji R, Othman TB, Alseraihy A, Abdel-Rahman F *et al.* Hematopoietic stem cell transplantation practice variation among centers in the Eastern Mediterranean Region (EMRO): Eastern Mediterranean Bone Marrow Transplantation (EMBMT) group survey. *Hematol Oncol Stem Cell Ther* 2013; **6**: 14–19.
13 Mohamed S, Fadhil I, Hamladji R, Hamidieh A, Fahmy O, Ladeb S *et al.* Hematopoietic stem cell transplantation in the Eastern Mediterranean Region (EMRO) 2008-2009: report on behalf of the Eastern Mediterranean Bone Marrow Transplantation (EMBMT) Group. *Hematol Oncol Stem Cell Ther* 2011; **4**: 81–93.
14 Aljurf M, Zaidi SZ, El Solh H, Hussain F, Ghavamzadeh A, Mahmoud HK *et al.* Special issues related to hematopoietic SCT in the Eastern Mediterranean region and the first regional activity report. *Bone Marrow Transplant* 2008; **43**: 1–12.
15 Bacigalupo A. Third EBMT/AMGEN Workshop on reduced- intensity conditioning allogeneic haemopoietic stem cell transplants (RIC-HSCT), and panel consensus. *Bone Marrow Transplant* 2004; **33**: 691–696.
16 Elbjeirami WM, Abdel-Rahman F, Hussein AA. Probability of finding an HLA-matched donor in immediate and extended families: the Jordanian experience. *Biol Blood Marrow Transplant* 2013; **19**: 221–226.
17 Jawdat DM, Al Saleh S, Sutton P, Al Anazi H, Shubaili A, Tamim H *et al.* Chances of finding an HLA-matched sibling: the Saudi experience. *BiolBlood Marrow Transplant* 2009; **15**: 1342–1344.
18 Shamsi T, Hashmi K, Adil S, Ahmad P, Irfan M, Raza S *et al.* The stem cell transplant program in Pakistan—the first decade. *Bone Marrow Transplant* 2008; **42**: S114–S117.
19 Hamidieh AA, Dehaghi MO, Paragomi P, Navaei S, Jalali A, Eslami GG *et al.* Efficiency of allogeneic hematopoietic SCT from HLA fully-matched non-sibling realtives: a new prospective of exploiting extended family search. *Bone Marrow Transplant* 2015; **50**: 545–552.
20 Hamamy H. Consanguineous marriages. *J Community Genet* 2012; **3**: 185–192.
21 Gaziev J, Marziali M, Isgro A, Sodani P, Paciaroni K, Gallucci C *et al.* Bone marrow transplantation for thalassemia from alternative related donors: improved outcomes with a new approach. *Blood* 2013; **122**: 2751–2756.
22 Rosenmayr A, Pointner-Prager M, Mitterschiffthaler A, Bozic L, Pelzmann B, Tüchler H *et al.* What are a patient's current chances of finding a matched unrelated donor rquest; twenty years' central search experience in a small country. *Bone Marrow Transplant* 2011; **47**: 172–180.
23 Aljurf M, Rizzo JD, Mohty M, Hussain F, Madrigal A, Pasquini MC *et al.* Challenges and opportunities for HSCT outcome registries: perspective from international HSCT registries experts. *Bone Marrow Transplant* 2014; **49**: 1016–1021.
24 Baldomero H, Gratwohl M, Gratwohl A, Tichelli A, Niederwieser D, Madrigal A *et al.* The EBMT activity survey 2009: trends over the past 5 years. *Bone Marrow Transplant* 2011; **46**: 485–501.
25 Weatherall DJ. Thalassemia as a global health problem: recent progress toward its control in the developing countries. *Ann NY Acad Sci* 2010; **1202**: 17–23.
26 Hussein AA, Al-Zaben A, Ghatasheh L, Natsheh A, Hammada T, Abdel-Rahman F *et al.* Risk adopted allogeneic hematopoietic stem cell transplantation using a reduced intensity regimen for children with thalassemia major. *Pediatr Blood Cancer* 2013; **60**: 1345–1349.
27 Modell B, Khan M, Darlison M. Survival in beta-thalassaemia major in the UK: data from the UK Thalassaemia Register. *Lancet* 2000; **355**: 2051–2052.

© 2017 Macmillan Publishers Limited, part of Springer Nature.

28 Rund D, Rachmilewitz E. Beta-thalassemia. *N Engl J Med* 2005; **353**: 1135–1146.
29 Ghavamzadeh A, Alimoghaddam K, Jahani M, Mousavi SA, Iravani M, Bahar B *et al.* Stem cell transplantation; Iranian experience. *Arch Iran Med* 2009; **12**: 69–72.
30 Mahmoud H, El-Haddad A, Fahmy O, El-Emary M, Nassar A, Abdel-Mooti M *et al.* Hematopoietic stem cell transplantation in Egypt. *Bone Marrow Transplant* 2008; **42**: S76–S80.
31 Amayiri N, Al-Zaben A, Ghatasheh L, Frangoul H, Hussein AA. Hematopoietic stem cell transplantation for children with primary immunodeficiency diseases: single center experience in Jordan. *Pediatr Transplant* 2013; **17**: 394–402.
32 Ayas M, Al-Jefri A, Al-Seraihi A, Elkum N, Al-Mahr M, El-Solh H. Matched-related allogeneic stem cell transplantation in Saudi patients with Fanconi anemia: 10 year's experience. *Bone Marrow Transplant* 2008; **42**: S45–S48.

Supplementary Information accompanies this paper on Bone Marrow Transplantation website (http://www.nature.com/bmt)

© 2017 Macmillan Publishers Limited, part of Springer Nature.