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Hematopoietic stem cell transplantation (HSCT) activity was surveyed in the 9 countries in the World Health Organization Eastern Mediterranean region that reported transplantation activity. Between the years of 1984 and 2007, 7933 transplantations were performed. The number of HSCTs per year has continued to increase, with a plateau in allogeneic HSCT (allo-HSCT) between 2005 and 2007. Overall, a greater proportion of transplantations were allo-HSCT (n=5761, 77%) compared with autologous HSCT (ASCT) (n=2172, 23%). Of 5761 allo-HSCT, acute leukemia constituted the main indication (n=2124, 37%). There was a significant proportion of allo-HSCT for bone marrow failures (n=1001, 17%) and hemoglobinopathies (n=885, 15%). The rate of unrelated donor transplantations remained low, with only 2 matched unrelated donor allo-HSCTs reported. One hundred umbilical cord blood transplantations were reported (0.017% of allo-HSCT). Peripheral blood stem cells were the main source of graft in allo-HSCT, and peripheral blood stem cells increasingly constitute the main source of hematopoietic stem cells overall. Reduced-intensity conditioning was utilized in 5.7% of allografts over the surveyed period. ASCT numbers continue to increase. There has been a shift in the indication for ASCT from acute leukemia to lymphoproliferative disorders (45%), followed by myeloma (26%). The survey reflects transplantation activity according to the unique health settings of this region. Notable differences in transplantation practices as reported to the European Group for Blood and Marrow Transplantation over recent years are highlighted.


INTRODUCTION

Hematopoietic stem cell transplantation (HSCT) is a potentially curative therapeutic modality for many hematologic and, increasingly, nonhematologic conditions. The last few decades have witnessed significant developments in conditioning techniques, better donor selection, and posttransplantation care, all of which have contributed to improvements in outcomes [1].

Data pertaining to transplantation are captured by a number of international registries, including the European Group for Blood and Marrow Transplantation (EBMT), International Bone Marrow Transplant Registry, World Bone Marrow Transplant Group, and Asia-Pacific Bone Marrow Transplant Group, among others. In addition to informing the transplant community of outcomes, risk factors, and efficacy of HSCT in given diseases, the information thus obtained also assists transplantation physicians in planning the various
components of transplantation programs and in directing research [2].

The Eastern Mediterranean Blood and Marrow Transplantation (EMBMT) group was conceived in 2007, and represents the 9 countries that have an active transplant program from among the 17 East Mediterranean Regional Organization (EMRO) nations as defined by the World Health Organization (WHO) (Table 1) [3]. We have recently reported on special issues pertaining to HSCT in the region such as the prevalence of hemoglobinopathies, cytomegalovirus seropositivity, prevalence of hepatitis B, and resource limitations. The report also provided a regional overview of economic status in terms of gross national income (GNI), transplantation rates, and team density [4]. In this report, we present a survey of HSCT activity pertaining to allogeneic HSCT (allo-HSCT) and autologous HSCT (ASCT) activity in the region over a 24-year period as reported to the EMBMT, and provide a comparison with transplantation activity reported to EBMT for 2007.

**METHODS**

The participating centers were identified by means of a database that was established following initial meetings between teams. An active program was identified as one that consistently performed ≥5 transplantations per year for at least 3 consecutive years. The EMBMT holds a directory of participating centers, with the names and addresses of participating centers and named transplantation physicians with their contact details.

An electronic data capture sheet was sent via e-mail to each of these members where the following fields of information were sought for allo-HSCT and ASCT transplants: indication of transplant (including stage of disease); conditioning in allo-HSCT (conventional versus reduced-intensity conditioning [RIC]); and source of stem cells (related bone marrow [BM] versus related peripheral blood stem cells [PBSC] versus umbilical cord blood [UCB] versus matched unrelated donor [MUD]).

The data were sought for each year since the inception of the respective transplant program. For transplant by indication, only the first transplantation was reported to avoid rereporting.

Data from different participating centers within a country were aggregated to present national data. The data were tabulated at the office of the EMBMT. No remuneration was offered to participating centers. The EBMT Group Activity Survey was utilized as a template for analysis of the activity data, and supplementary data was obtained from EBMT as needed. The reported data was also matched with submitted data for the Center for International Blood and Marrow Transplant Research (CIBMTR) for CIBMTR reporting centers. A comparison was made between transplant practices in the EMBMT survey for 2007 and HSCT activity reported to the EBMT for the same year.

**RESULTS**

**Overall Transplant Activity**

Countries identified with an active transplant program were Egypt, Iran, Jordan, Lebanon, Morocco, Oman, Pakistan, Saudi Arabia, and Tunisia. Of 17 active teams in 9 countries, completed data capture sheets were received from all except 2 teams (Makassed General Hospital, Lebanon, and Bismilah Taqi Institute, Pakistan). Information on the type of conditioning was not available from 2 countries (Tunisia and Iran). Information on the source of stem cells was incomplete from 2 countries (Pakistan and Tunisia).

A total of 7933 first transplantations were reported between the periods of 1984 and 2007, of which 2172 (27%) were ASCTs and 5761 (73%) were allo-HSCTs (Table 1). There was an increase in overall transplant

<table>
<thead>
<tr>
<th>Country</th>
<th>Age of Program (Years)</th>
<th>No. of Procedures</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ASCT</td>
<td>Allo-HSCT</td>
</tr>
<tr>
<td>Egypt</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Iran</td>
<td>16</td>
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</tr>
<tr>
<td>Lebanon</td>
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</tr>
<tr>
<td>Morocco</td>
<td>3</td>
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</tr>
<tr>
<td>Oman</td>
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<tr>
<td>Pakistan</td>
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<td>6</td>
</tr>
<tr>
<td>Tunisia</td>
<td>8</td>
<td>10</td>
</tr>
<tr>
<td>Total number of transplantations:</td>
<td>2172</td>
<td>5761</td>
</tr>
</tbody>
</table>

ASCT indicates autologous hematopoietic stem cell transplantation; allo-HSCT, allogeneic hematopoietic stem cell transplantation; EMBMT, Eastern Mediterranean Blood and Marrow Transplantation; KSA, Kingdom of Saudi Arabia.

*EMRO countries that do not have a transplant program, or that were not reported to the EMBMT to have performed ≥5 HSCT for ≥3 years were: Afghanistan, Bahrain, Djibouti, Iraq, Kuwait, Libya, Qatar, Somalia, Sudan, Syria, United Arab Emirates, Yemen.
activity from 12 transplantations in 1984 to 1097 in 2007 (Figure 1). Over the survey period, the mean year-on-year increase in transplant activity was 24%, with a significant increase in activity in the period 1996 to 2007.

Allogeneic Transplantation

A total of 5761 allo-HSCT procedures were performed, starting with 12 in 1984 to 684 in 2007. Except for Morocco, where all reported transplantations were ASCT, and Tunisia, where 50% of transplantations were ASCT, in the remaining countries the majority of the transplants were allo-HSCT (Figure 2). There was significant variation in total allo-HSCT number between countries and in the increase in numbers over the 24-year period (Table 1 and Figure 3). Over 2005 to 2007, overall allo-HSCT numbers showed a plateau, although numbers in Iran and Pakistan continue to rise.

Indication for Allogeneic Transplantation

Of the 5761 allo-HSCTs, a major indication was acute leukemia (n = 2124, 36.8%). Acute myeloid leukemia (AML) accounted for 1260 (21%) allo-HSCTs with 924 transplantations in first complete remission (CR1) (16%) and 336 (5%) beyond CR1. Acute lymphoblastic leukemia in all stages accounted for 864 (15%) allo-HSCTs. Other major indications were bone marrow failure, both congenital and acquired (n = 1001, 17%), followed by chronic myeloid leukemia (CML) in both chronic phase and beyond (n = 948, 16%). There was a recent reduction in allo-HSCT for CML (Figure 4). There was a significant proportion of patients who received transplants for hemoglobinopathies (n = 885, 15%), especially in Iran and Egypt, which both have a high carrier rate of β-thalassemia [5,6]. Other diagnoses were the indication for allo-HSCT in the remaining 15% of reported cases, and indications remained relatively stable over time (Figure 5).

Conditioning Regimes

Conditioning information was sought for all allo-HSCTs. Of the 8 countries performing allo-HSCTs, data were returned from 5. Of all 5761 allo-HSCTs, 3483 (60.4%) were performed with conventional conditioning regimes, and 333 (5.7%) utilized RIC. Conditioning intensity was unknown in 1945 (33.7%) allografts.

RIC transplants, although not performed before 1999, are being performed increasingly and accounted for conditioning in 51 transplants in 2007 (Figure 6). Over the survey period, the mean annual proportion of RIC HSCT was 13.4% of allo-HSCTs where conditioning information was available.

Stem Cell Source for Allogeneic Transplants

The sources of hematopoietic stem cells for allo-HSCTs were peripheral blood stem cells (PBSCs) (2688 allo-HSCTs, 47%) followed by BM (2523 allo-HSCTs, 44%). The source was unknown in 478 (8.2%) allo-HSCTs. There was a shift from BM to PBSCs, especially in the years after 2000 (Figure 7). There were variations between countries in the use of BM versus PBSCs. In the Kingdom of Saudi Arabia, related BM was used in 1815 (86%) of allo-HSCTs over the surveyed period, while in Egypt, BM was the source in only 31 (3%), with PBSCs being used in 97% of allo-HSCTs. In the other countries surveyed, PBSCs were used more frequently than BM.
UCB transplantations were first performed in the region in 1998. Overall, 100 transplantations (2% of allografts) have been performed with UCB as a source of stem cell. There were 6 coinfusions of BM with PBSCs (5/6) and UCB (1/6). Only 2 (0.003%) non-UCB MUD allo-HSCTs were reportedly performed.

### Autologous Transplantation

A total of 2172 ASCT procedures were performed during the period 1985 to 2007. There was an increase in procedures from 1 in 1985 to 413 in 2007 with a continuing increase in transplantation procedures year-on-year. There was a 25% increase in ASCT activity from 2006 to 2007 (Figure 1).

#### Indication for Autologous Transplantation

Of the 2172 total ASCTs, the main indications were myeloma (n = 557, 25.6%), Hodgkin’s lymphoma (n = 539, 25%), non-Hodgkin lymphoma (n = 451, 20.7%), and AML (n = 326, 15%), with other indications comprising the remaining 14% of ASCTs. There was a reduction in the proportion of ASCTs performed for

![Figure 2](image)

**Figure 2.** Overall autologous and allogeneic hematopoietic stem cell transplantation numbers, 1984 to 2007, by country. Abbreviations: KSA indicates Kingdom of Saudi Arabia; ALLO-HSCT, allogeneic hematopoietic stem cell transplantation; ASCT, autologous stem cell transplantation.

![Figure 3](image)

**Figure 3.** Trends in total numbers of first allo-HSCT activity, 1984 to 2007, by country as reported to EMBMT. Abbreviations: Allo-HSCT indicates allogeneic hematopoietic stem cell transplantation; EMBMT, Eastern Mediterranean Blood and Marrow Transplantation; KSA, Kingdom of Saudi Arabia.
acute leukemia and myelodysplasia from a median of 70.5% (range: 50%-100%) in the years 1988 to 1996, to 21% (10%-46%) in the years 1997 to 2007 (Figure 8).

A total of 32 ASCTs were performed between the years of 1996 and 2001 for breast cancer; none were reported for this indication after 2001. ASCT

Figure 4. Trends in allo-HSCT for CML in first chronic phase (CP1) and beyond (>CP1). Abbreviations: Allo-HSCT indicates allogeneic hematopoietic stem cell transplantation; CML, chronic myeloid leukemia.

Figure 5. Trends in allo-HSCT in the Eastern Mediterranean region by disease indication, 1984 to 2007, expressed as percentage of annual transplants. Abbreviations: AML indicates acute myeloid leukemia; ALL, acute lymphoblastic leukemia; CML, chronic myeloid leukemia; MDS, myelodysplasia; MPD, myeloproliferative disorder; LPD, lymphoproliferative disorders; BMF, bone marrow failure.
procedures were performed in a total of 134 (6%) cases of other nonhematologic malignancies.

**Stem Cell Source for Autologous Transplants**

PBSC was the main source of stem cells in 1875 (86%) ASCTs; BM was the source for 223 (10%) ASCTs, and in 11 (1%) both PBSCs and BM stem cells were co-infused. The source of stem cells was not known in 65 (3%) ASCTs.

**DISCUSSION**

This is the first activity survey of the EMBMT, which presents the analysis of transplantation activity in the WHO EMRO region between the years 1984 and 2007. Individual country reports have previously been published, highlighting each country’s unique HSCT setting. The data here illustrate the increasing transplantation activity in the region over the years and
the trends in indication for HSCT conditioning practices and sources of stem cells.

The overall number of transplantations in the EMRO region of 7933 over a span of 24 years is significantly lower as a cumulative number compared with annual numbers in Western Europe over a single year. In 2003, 17,020 first HSCTs were performed in 15 Western European countries with a population of 381 million, equating to 446 HSCTs per 10 million population [7]. In comparison, in the 9 EMBMT countries with a collective population of 367 million in the same year [8], 704 HSCTs were performed, or 19 per 10 million population. However, transplantation numbers, especially ASCTs, in the region continue to increase at a steady rate and have yet to plateau, although transplantation rates remain low [4].

Factors that may contribute to regional differences in HSCT activity have been elucidated [9,10]. Allo-HSCT is an expensive procedure, and various factors can affect total cost [11]. GNI, team density, and healthcare expenditure reportedly have an impact on transplantation numbers [12].

Although there appears to be a degree of correlation between GNI and stem cell transplantation per 10 million inhabitants, this does not always hold true, and various other unexplained factors are likely to contribute to a higher or lower than expected HSCT rate in any given country (Figure 9). There may be a number of reasons for discrepancies in transplantation rates in countries with similar GNI, including infrastructure and sociopolitical factors [9,13]. Data for patients referred overseas for HSCT were not available for the purposes of the study, although such referral practices may go some way in fulfilling transplantation requirements, especially in the few countries with a higher GNI.

**Allo-HSCT versus ASCT**

There has been a steady increase in the number of allo-HSCTs being performed with a mean year-on-year rise of 20%. There was no significant overall increase over the period 2005 to 2007, possibly as a reflection of the saturation of available services or other local factors.

The majority (73%) of all transplantation procedures over the survey period were allo-HSCT, and this was true for each year surveyed (mean: 74%, range: 63%-100%). In 2007, 63% of procedures were allo-HSCT, representing a gradual trend toward an increase in the proportion of ASCTs. This is in contrast to activity reported from EBMT, where in 2007 ASCTs comprised the majority of transplantation activity with 15,491 (61%) ASCTs versus 10,072 (39%) allo-HSCTs [14]. Data from the United States as reported to CIBMTR also demonstrate an excess of ASCT over allo-HSCT [15]. A possible explanation for the excess allo-HSCTs may be that the Eastern Mediterranean region consists of communities of large families with high population growth, which certainly

**Figure 8.** Trends in ASCT in the Eastern Mediterranean region by disease indication, 1984 to 2007, expressed as percentage of annual transplants. Abbreviations: AML indicates acute myeloid leukemia; ALL, acute lymphoblastic leukemia; CML, chronic myeloid leukemia; MDS, myelodysplasia; MPD, myeloproliferative disorder; PCD, plasma cell disorders; NHL, non-Hodgkin lymphoma; HD, Hodgkin’s disease; CLL, chronic lymphocytic leukemia; PLL, prolymphocytic leukemia.
increases the likelihood of finding a full matched sibling donor. Demographic information of the transplanted population in the EMRO region would be required to investigate this regional difference further. Consistent with practices worldwide, there have been no ASCTs for breast cancer following 2001, after studies failed to show a survival benefit in these patients [16,17].

Indications and Diseases

The main indications for allo-HSCT remain acute leukemias and BMF syndromes. In 2007, allo-HSCT for BMF syndromes was proportionally a more common indication for HSCT in the EMBMT data (n = 106, 15% of allo-HSCT) compared with EBMT data (n = 523, 5%) [14]. Whether this is because of differences in the incidence of diseases or other causes remains to be determined, although data on large cohorts of patients with inherited BMF in the Middle East have been published [18].

In our survey, hemoglobinopathies were the indication for allo-HSCT in 874 cases, comprising 15.2% of all allo-HSCTs. There was considerable variability in the proportion transplanted for this indication. In both Iran and Pakistan, hemoglobinopathies were the indication for allo-HSCT in 30% of all transplants, and their respective experiences have been reported [19,20]. In 2007, 102 of 684 (14.9%) transplants were performed in the Eastern Mediterranean region for this indication. In contrast, this was an indication in only 2.7% of transplants reported to EBMT in 2007 (Table 2) [14].

There has been a worldwide decline in the use of HSCT for the treatment of CML in first chronic phase with the advent of imatinib mesylate [15,21,22]. Although this recent reduction is observed in our survey, it is noteworthy that CML still constituted an indication for allo-HSCTs in 60 (8.7%) cases in 2007 compared with 0.4% for 2007 in the EBMT survey for that year [14]. This may be partly because of limited access to tyrosine kinase inhibitors in some countries, but may also reflect demographic differences that were not analyzed in this activity survey.

Stem Cell Source Trends

The trend toward increased use of PBSC in both allo-HSCT and ASCT is consistent with practice as reported by the National Marrow Donor Program (NMDP) and EBMT activity surveys [23,24]. In our survey, in 2007, 65% of all allo-HSCTs were PBSC derived, followed by related BM (25%) and UCB (4%). PBSCs are logistically less burdensome to procure and entail a lower likelihood of complications for donors, obviating the need for general anesthesia. The increasing trend has not been influenced by evidence to suggest a higher incidence of graft-versus-host disease [25-27].

Although there has been an increase in the use of UCB as a stem cell source—a trend observed in Europe [28]—and although there are established cord banks in the region, these provide a source of stem cells in only a minority (2%) of transplantations (Figure 7). Unrelated donor transplants are exceedingly uncommon in the EMBMT region, and only 2 nonumbilical cord MUD transplantations have been reported. This is in marked contrast to data reported to the EBMT, where in 2007, 4752 HSCT (47%) were performed with an unrelated donor source (Table 2). Larger family sizes and the higher probability of finding an HLA-matched sibling donor, the possibility of a parent being a match because of consanguinity and intermarriage, and the availability of HLA-matched nonsibling related donors all contribute to reducing the need for a UCB or MUD transplant [4].
Although complete data pertaining to conditioning were lacking, most of the reported allo-HSCTs were performed with conventional conditioning, with RIC being used in no more than 20% of transplantations in any given year. In contrast, the EBMT survey demonstrated that RIC was utilized in 36% of all allo-HSCT in 2007, and is reportedly as high as 71% in some European countries [14,22]. The increase in RIC HSCT in our survey in the years between 1999 and 2001 corresponds temporally to a similar rise as reported to EBMT, although the numbers in our survey are smaller. Data regarding the indications for RIC transplantations per se were not requested in our survey. Further studies, including demographic information regarding the age and/or comorbidities of patients, may help in elucidating the reason for this discrepancy between EBMT and EMBMT data with regard to RIC allo-HSCT. The disparity may also be a reflection of the differences in proportions of indications for HSCT in the registries.

CONCLUSIONS

This report demonstrates the unique transplantation practices for a region where transplant numbers continue to rise. We also demonstrate that there is a marked difference in transplantation indications as reported to EMBMT compared with data reported to EBMT with relatively larger proportions of stem cell transplantations being performed for hemoglobinopathies and bone marrow failure syndromes in the former. Further retrospective studies focusing on these conditions may be a valuable contribution of the EMBMT to the international HSCT community. A further contrast that requires study is the higher proportion of allo-HSCT versus ASCT, and reduced utilization of alternate donors and of RIC transplantations, although data for the latter was incomplete. The current survey did not study patient demographics or outcomes, as these data were not sought for the purposes of this activity survey. It is important to note that because a number of countries comprising the EMBMT reported to EBMT (Iran, KSA, Lebanon, Tunisia) and CIBMTR (Egypt, Iran, Pakistan, Saudi Arabia) in 2007, differences in HSCT activity between the registries, while reflecting regional differences, represent data as made available to the registries.

The increasing rates of transplantation will require adequate planning for resources in the future, not least with regard to ensuring adequate numbers of transplantation physicians and nurses to deal with increasing transplant demands [29].
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