

Stem Cell Transplantation in Iran; 1991 until 2009

A. Ghavamzadeh¹, K. Alimogaddam¹, M. Jahani¹, S.A. Mousavi¹, M. Iravani¹, B. Bahar¹, A. Khodabandeh¹, F. Khatami¹, A. Jalali¹
¹Hematology-Oncology and Stem Cell Transplantation Research Center, Tehran University of Medical Sciences, Shariati Hospital, Tehran, Iran

Corresponding author: Kamran Alimoghaddam

Phone number: +98 21 84902668

Fax number: +98 21 88004140

E-mail: alimgh@sina.tums.ac.ir, alimgh@ams.ac.ir

Abstract

Hematology- Oncology and Stem Cell Transplantation Research Center related to Tehran University of Medical Sciences located in Shariati Hospital. These center activities have started in 1991 in order to help needful patients and augment new data to reach new aspects of therapeutic trials. Also it is one of the greatest Stem Cell Transplantation centers in world and is the second center in the world based on the transplanted Thalassemia patients. Since 1991, 2426 first Hematopoietic Stem Cell Transplantation (HSCT) has been performed in patients with different diseases. Acute Myelogenous Leukemia (647 patients), Thalassemia Major (386 patients) and Acute Lymphoblastic Leukemia (335 patients) were the most common transplanted disorders, respectively. There were 1662 cases that have received allogeneic HSCT and 764 cases that have received autologous HSCT. Number of allogeneic ant autologous HSCT is increased during the time, but the allogeneic to autologous ratio remains constant. The first peripheral blood Hematopoietic Stem Cell Transplantation was performed in 1996 and since then, there was 1988 patients were done with this method. The donor types for 1662 allogeneic first HSCT were 1577 (94.9%) Human Leukocyte Antigen (HLA) matched-identical siblings, 44 (2.6%), HLA mismatched sibling/other relative, 16 (1%) syngeneic twins, 18 (1.1%) HLA matched other relative and 7 (0.4%) unrelated. The first cord blood Hematopoietic Stem Cell Transplantation was performed in 1998 and since then there was 16 patients that have obtained cord blood transplantations. Recently, new methods have been used like Donor Lymphocyte Infusion (DLI) and Cellular Therapy. There were 147 patients with Cellular Therapy for post MI, Cirrhosis, Thalassemia major, Multiple Sclerosis, Head of Femour Necrosis and GvHD treatment.

Keywords: Allogeneic, Autologous, Stem Cell Transplantation, Thalassemia, Hematologic Malignancies

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Introduction

Bone marrow transplantation was the original term used to describe the collection and transplantation of hematopoietic stem cells, but with the recent demonstration that the peripheral blood and umbilical cord blood are also useful sources of stem cells, hematopoietic cell transplantation has become the preferred generic term for this process. The procedure is usually carried out for one of two purposes: (1) to replace an abnormal but nonmalignant lymphohematopoietic system with one from a normal donor, or (2) to treat malignancy by allowing the administration of higher doses of myelosuppressive therapy than would otherwise be possible. The use of bone marrow transplantation has been steadily increasing, both because of its demonstrated effectiveness in selected diseases and because of increasing availability of donors. The

International Bone Marrow Transplant Registry estimates that about 50,000 transplants are performed each year.(1, 2) Hematology- Oncology and Stem Cell Transplantation Research Center related to Tehran University of Medical Sciences located in Shariati Hospital. Performed the first HSCT in Iran in 1991 by professor Ardeshir Ghavamzadeh et al. and carrying out this treatment for different kinds of cancers and hematological disorders. This center is one of the Center for International Blood and Marrow Transplantation Registry (CIBMTR) and European group of Blood and Marrow Transplantation (EBMT) member and in accompanys with these associations, is gathering the patient's databases who have been undergone transplantation; and cooperate with these centers in scientific and research fields. This center is the member of Asian Pacific Cancer Center (APCC)

and also has collaborating with Blood and Cancer Associations such as American Society of Hematology (ASH), International Society of Hematology (ISH), and European School of Medical Oncology (ESMO), American Society of Clinical Oncology (ASCO), and other centers. The plans and aims include protraction of cytogenetic and molecular biological diagnostic tests, invention of a cord blood bank and develop the research activities in this fields.(3)

Patients and methods

From March 1991 till January 2009 patients were undergone Hematopoietic Stem Cell Transplantation in Hematology- oncology and Stem Cell Transplantation Research Center. Product types were from Bone Marrow, Peripheral Blood, Cord Blood, combining Bone Marrow and Peripheral Blood, and Mesenchymal origins.(4, 5) According to patients' states, we used allogeneic, autologous or syngeneic stem cell grafts.(6) All patients were treated in completely isolated rooms during the peri-transplant period. It was conventional private and HEPA filtered room with at least entertainment home appliances to avoid depression. Stem cells were obtained and kept at 4°C (centigrade) for 1-4 days before reinfusion. The stem cells were reinfused without purging.(7) Hematology- Oncology and Stem Cell Transplantation Research Center has a research office that a section for data management consist of gathering the Stem Cell Transplantation data of Stem Cell Transplantation wards, checking reports for completeness of data and identifying missing data, reporting missing fields and after completing them, entering Report Forms into the computer database program for statistical analysis and preparation of statistical reports and finally sending requested information to CIBMTR, EBMT and HSCT in the Eastern Mediterranean Region.(8) This office is also responsible for quality control of data entry processes and training patients, Stem Cell Transplantation and data management staff. Iran has a population of about 70 million people. The incidence of transplantable diseases is estimated at about 2 per 100000 or 1400 patients per year. The cost of transplant procedures is borne by insurance companies and board of trustees.

Definitions: Hematopoietic Stem Cell Transplantation number indicates the numbers of patients treated for the first time with Hematopoietic Stem Cell Transplantation. Transplant rate were defined as number of HSCTs

per 1 million inhabitants.(9) Population data have been achieved from Statistical Center of Iran (www.sci.org.ir). Re-transplant was determined as an unplanned HSCT for rejection or relapse after a first HSCT. Donor Lymphocyte Infusion (DLI) is a method to treatment of patients with recurrent or persistent malignancy after allogeneic HSCT with infusion of additional lymphocyte obtained from the original donor, without the cover of immunosuppressive agents.(10) Cell therapy is a technology that relies on replacing diseased or dysfunctional cells with healthy, functioning ones.

Results

The first stem cell transplantation in Hematology-Oncology and Stem Cell Transplantation research center was performed in March 3th, 1991. From 1991 till December 31, 2008, a total of 2426 first Hematopoietic Stem Cell Transplantation was carried out (Figure 1). This figure shows HSCT has increased tenfold in compared to last decade. The Hematopoietic Stem Cell Transplantation rate during the past 18 years was 38.4 transplants per one million inhabitants. Also the rate of HSCT has increasing from 1991 till 2009 (Figure 2).

From 2426 first transplantations 1662 (68.5%) were Allogeneic and 764 (31.5%) were Autologous HSCT (Figure 3). Number of allogeneic ant autologous HSCT is increased during the time, but the allogeneic to autologous ratio remains constant (Figur 4).

From 1662 allogeneic first HSCT, there was 1293 (77.8%) Peripheral Blood, 303 (18.2%) Bone Marrow, 8 (0.5%) combined Peripheral Blood and Bone Marrow, 42 (2.5%) mesenchymal with Bone Marrow or Peripheral Blood and 16 (1%) Cord Blood as product types. Of 764 autologous patients with first HSCT, 695 (91%) received Peripheral Blood, 65 (8.5%) Bone Marrow and 4 (0.5%) mixed Bone Marrow and Peripheral Blood as stem cell sources (Figure 5).

The donor types for 1662 allogeneic first HSCT were 1577 (95%) HLA matched-identical siblings, 44 (2.6%) HLA mismatched sibling/other relative, 16 (0.9%) syngeneic twins, 18 (1.1%) HLA matched other relative and 7 (0.4%) unrelated. The first cord blood Hematopoietic Stem Cell Transplantation was performed in 1998 and since then there are 16 patients that have obtained cord blood transplantations. The most frequent cord blood transplantations were in 2004. All of the cord blood HSCT was Allogeneic and there was no autologous cord blood HSCT.

Figure 1. Number of Hematopoietic Stem Cell Transplantation from 1991 to 2009

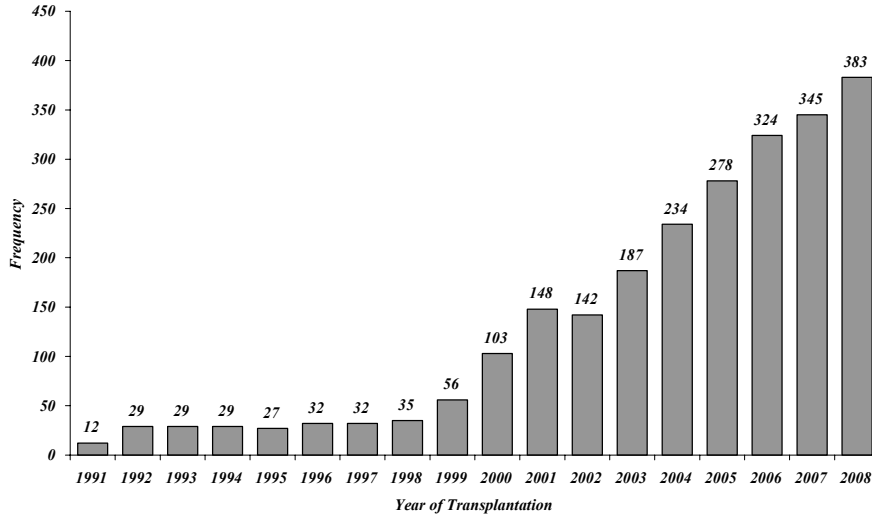


Figure2. Total Rate of Hematopoietic Stem Cell Transplantation during the past 19 years

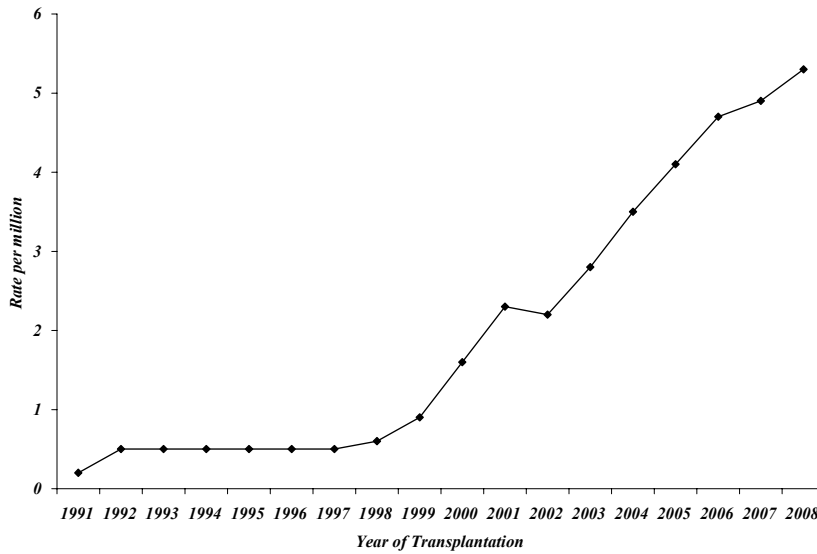
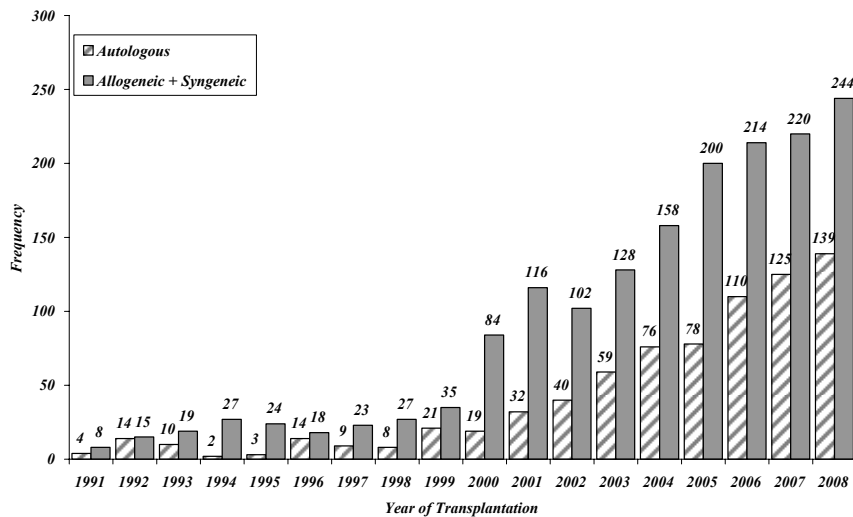


Figure3. Number of Allogeneic & Autologous Hematopoietic Stem Cell Transplantation



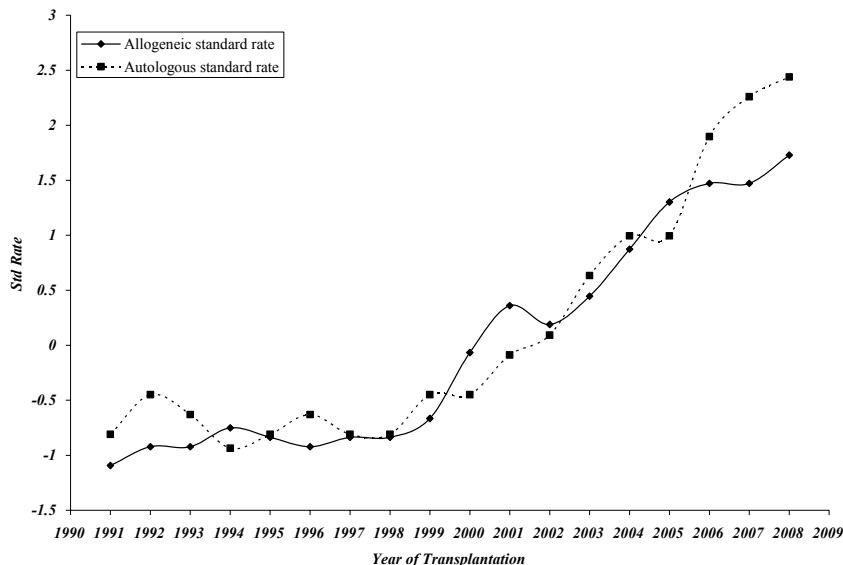


Figure 4. Standardized Rate of Allogeneic & Autologous Hematopoietic Stem Cell Transplantation in the past 18 years

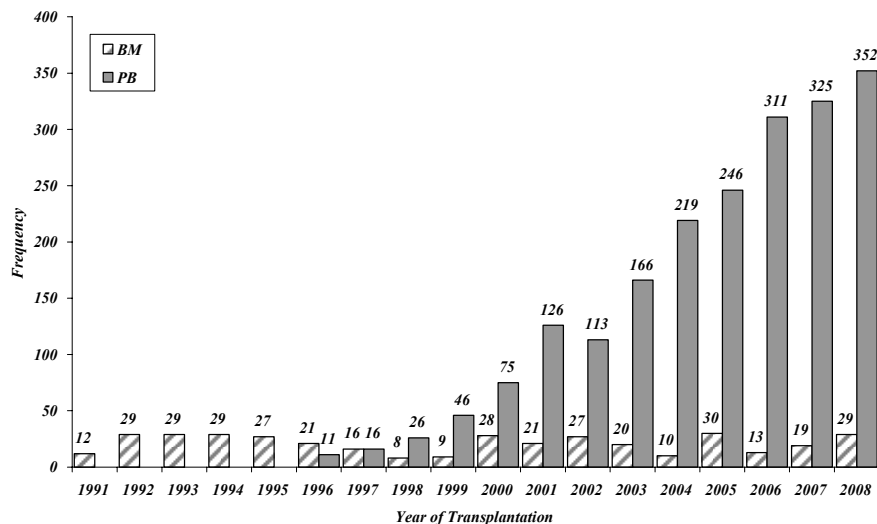


Figure 5. Number of Peripheral Blood & Bone Marrow Hematopoietic Stem Cell Transplantation

The primary diseases for which transplant were performed is in Table 1. Main diseases are Acute Myelogenous Leukemia with 647 patients (26.7%), 438 (67.7%) with Allogeneic HSCT, 209 (32.3%) with autologous HSCT; Thalassemia major with 386 allogeneic patients (16%); Acute Lymphoblastic Leukemia with 335 patients (13.8%), 310 ones (92.5%) with allogeneic HSCT, 25 ones (7.5%) with autologous HSCT; Lymphomas with 304 patients (12.5%), 35 ones (11.5%) with allogeneic HSCT, 269 ones (88.5%) with autologous HSCT; Chronic Myelogenous Lymphomas, with 231 allogeneic patients (9.5%); Multiple Myeloma, with 205 patients (8.5%), Sever Aplastic Anemia, with 144 patients (6%) and other uncommon diseases in 7 % of patients.(11) In Acute Myelogenous Leukemia and Acute Lymphoblastic Leukemia patients the Allogeneic

HSCT is more than Autologous HSCT. Patients with Lymphoms, Multiple Myeloma, Plasma Cell Disorders and Solid tumors approximately received Autologous HSCT. On the other hand patient with Chronic Myelogenous Leukemia, Sever Aplastic Anemia, Hemoglobinopathies, Disorder of Immune system, Myelodysplasia and Inherited disorder of Metabolisms just treated with Allogeneic HSCT. Auto-Immune diseases are indications with only Autologous HSCT. Acute Myelogenous Leukemia, Thalassemia Major and Acute Lymphoblastic Leukemia were the most common transplanted disorders, respectively.(12) Acute Myelogenous Leukemia shows a fixed increase in both Allogeneic and Autologous HSCT (Figure 6a) and the allogeneic to autologous ratio is stable (Figure 6b).

Figure6. a. Evaluation of Hematopoietic Stem Cell Transplantation Number by graft type for AML patients, b. Standardized number of Allogeneic & Autologous hematopoietic stem cell transplantation for AML patients

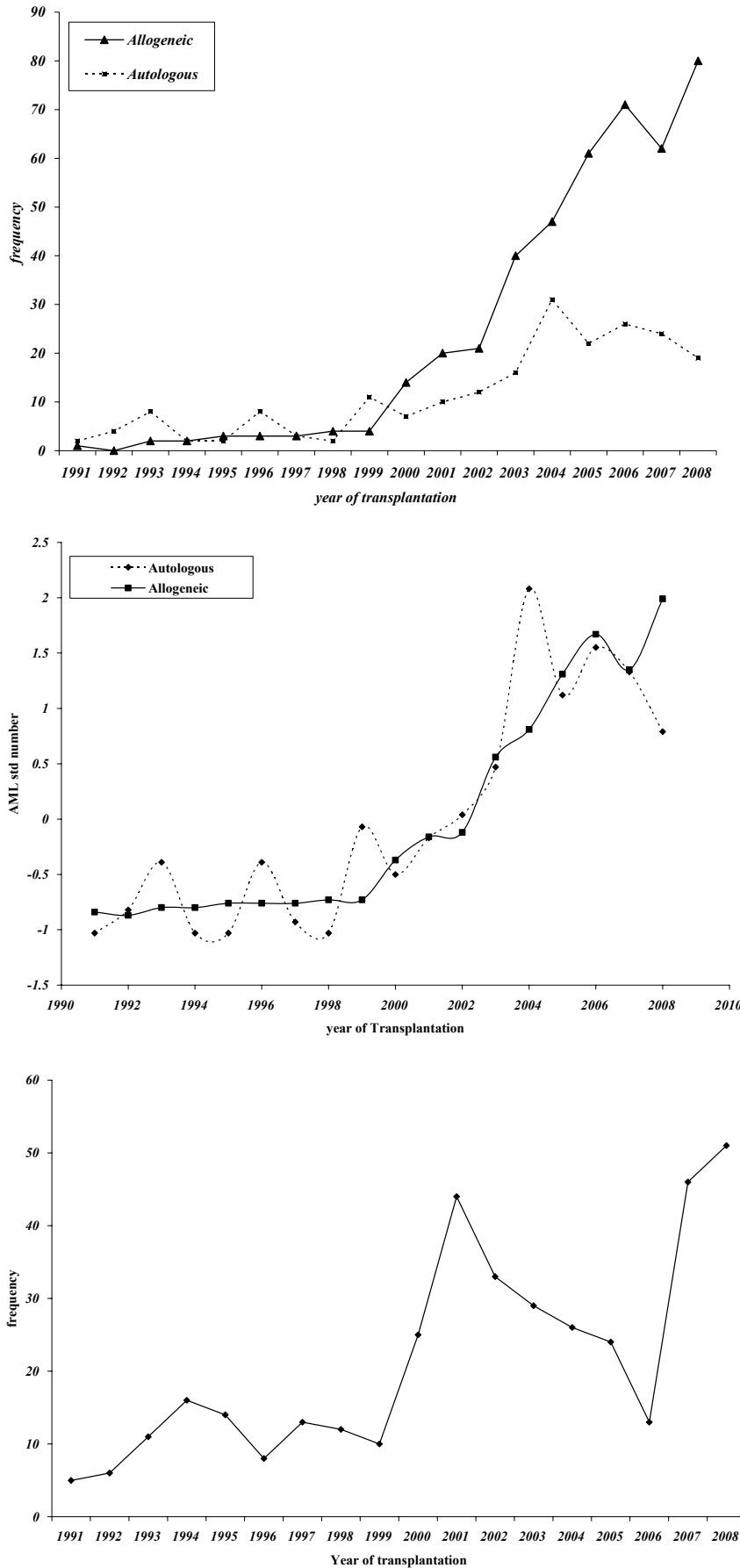


Figure7. Evaluation of Hematopoietic Stem Cell Transplantation number for Thalassemia patients

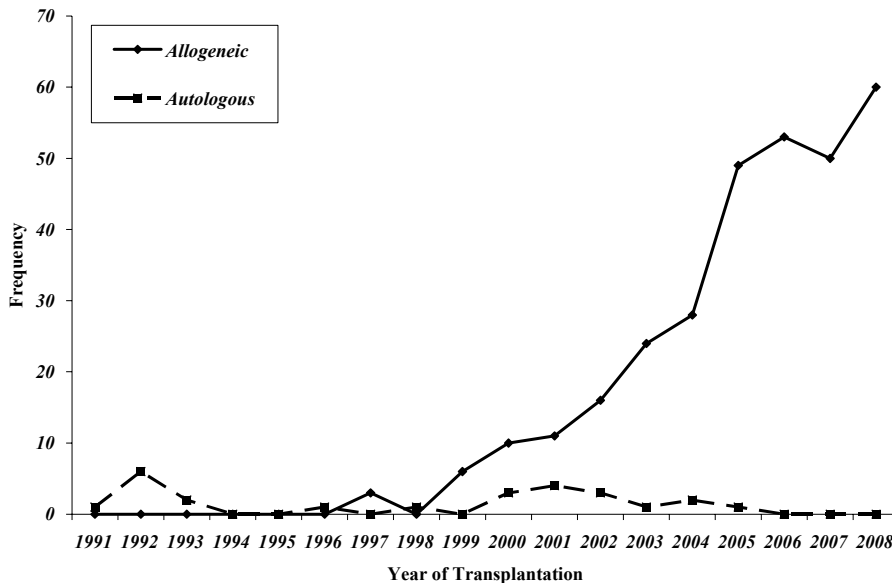


Figure8. Evaluation of Hematopoietic Stem Cell Transplantation number by graft type for ALL patients

Thalassemia Major indicates a peak in 2001 then a rapid decline till 2006 and after that there was further growth (Figure 7). Acute Lymphoblastic Leukemia initially started with Autologous HSCT in 1991 then the Allogeneic HSCT augment in 1995 and thereafter there was an increase in Allogeneic HSCT with stable low numbers for autologous HSCT (Figure 8). There were 95 patients that have

Table 1. Number of patients with a first Hematopoietic Stem Cell Transplantation listed by Diseases

Specific Disease	Graft type		Total
	Autologous	Allogeneic	
AML	209	438	647
ALL	25	310	335
Other Leukemia		7	7
CML		231	231
Multiple Myeloma	202	3	205
Plasma Cell Disorder	10	1	11
Lymphomas	269	35	304
Solid tumors	43	6	49
Severe Aplastic Anemia		144	144
Thalassemia Major		386	386
Inherited Abnormalities of RBC		41	41
Auto-Immune Diseases	5	0	5
Inherited disorder of Metabolism		4	4
Disorder of Immune system		18	18
Histiocytic Disorders		2	2
MDS/MPS	1	36	37
Total	764	1662	2426

received Donor Lymphocyte Infusion (DLI). Some patients obtained DLI more than once. The total number of DLI procedure was 129 that the most frequency of it was in 2006. During the past 18 years 33 patients were retransplanted. The common disorders in retransplanted patients were Thalassemia major, Acute Leukemias, Lymphomas, Multiple Myeloma and Sever Aplastic Anemia respectively. Cellular Therapy was done for 147 patients, 47 patients were post Myocardial Infarction, 29 ones Cirrhosis, 42 ones Thalassemia major, 11 ones Multiple Sclerosis, 14 ones Head of Femour Necrosis and 4 patients for GvHD treatment.

Discussion

Hematopoietic Stem Cell Transplantation is a choice treatment of many malignant, nonmalignant and genetic diseases. According to statistical reviewing during the past 18 years in Hematology-Oncology and Stem Cell Transplantation Research Center, Hematopoietic Stem Cell Transplantation number and rate have development especially after year 2000. It is considerable that transplant rate for allogeneic HSCT was more than Autologous HSCT, but both of them have increasing with stable ratio. It is interpretative that the number of HSCT for Acute Myelogenous Leukemia and Acute Lymphoblastic Leukemia was more frequent among all disorders; also the predominant type of HSCT in these diseases was Allogeneic, that is similar to the European Group for Blood and Marrow Transplantation (EBMT) survey.(13) Peripheral blood was the main source of Hematopoietic Stem Cell transplantation and it was the same as EBMT survey.(14) The most frequent donor type was

allogeneic full HLA-matched siblings. The plans and aims include protraction of cytogenetic and molecular biological diagnostic tests, invention of a cord blood bank and development of research activities in these fields. This center's future planned studies are: Transplants for Breast cancer, Neuroblastoma, Ewing sarcoma, soft tissue sarcom, Allogeneic Hematopoietic Stem Cell Transplantation for Renal Cell Cancer, Allogeneic Hematopoietic Stem Cell Transplantation for colorectal carcinoma. Also Cell Therapies for Post Myocardial Infarction, Cirrhosis, Thalassemia Major, Multiple Sclerosis, Head of femur necrosis, Sever Aplastic Anemia and GvHD treatment.

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