

Establishing A Successful Bone Marrow Transplant Program In A Resource-Constraints Rural Area

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Abstract

Objective: To evaluate the challenges, strategies, and outcomes involved in establishing and running a Bone Marrow Transplant (BMT) program in a resource-constrained rural area, with a focus on infrastructure development, human resource capacity building, and collaborative efforts for sustainable success

Study design: A Descriptive cross-sectional observational study.

Study Place & Duration: Gambat Institute of Medical Sciences (GIMS) from Jan 2021 to March 2021

Methods: A large size public sector facility was established in remote area of interior Sindh province of Pakistan. The program involved construction of infrastructure, human resource development, and setting up of building maintenance protocols. The essential steps involved in its establishment were human resource capacity building and teamwork.

Results and Conclusion:

Establishing and successful BMT program in the public sector in resource-limited setting is a difficult task that needs a vibrant administrative support, involvement of experienced person to lead the facility and twining with some advanced center for initial human resource development. Resource constraintsnations may have a somewhat higher incidence of complications due to socioeconomic variables and increased infection risks. While transplantation has the ability to satisfy unmet medical needs, future collaborations headed by experienced transplantation facilities will be required for the development and extension of BMT in the poor countries.

Keywords: Bone marrow transplantation, malignant hematological disorders.

INTRODUCTION

Hematopoietic stem cell transplantation (HSCT) is curative treatment for numerous congenital and acquired blood diseases. Over the past three decades there has been exponential growth in HSCT due to introduction of modern technologies, use of peripheral blood stem cells, establishment of stem cell donor registries, and implementing low-intensity conditioning regimens for elderly patients.¹⁻⁵ There is evidence for usefulness of BMT in numerous malignant hematological conditions, inherited and acquired bone marrow failure syndromes, hemoglobinopathies and immunodeficiency states.⁶⁻¹⁰ Cost of allogeneic and autologous HSCT varies from 7000 \$ to 15000 \$.¹¹ In addition to financial support, successful BMT requires specialized facilities, skilled human resource, innovative diagnostics, and pharmacological and biological products. There is marked difference in HSCT frequency per million population between developed and low-income countries. Gratwohl et al.¹² did a comprehensive analysis of rate of BMT per million people and discovered a direct correlation with growing levels of GDP per capita, public health expenditures, and the human development. However, despite being costly and technically challenging, several low-income countries

have reported establishment of successful autologous and allogeneic BMT programs.¹³⁻¹⁷ Considering the entire cost of care over time for certain chronic debilitating diseases such as transfusion-dependent thalassemia in children; with HSCT as a cure, may make it a financially feasible alternative to current treatment methods.¹⁷

HEALTH CARE IN PAKISTAN:

Competition between formal and informal commercial healthcare systems, as well as the country's federal and provincial government healthcare subsystems, contributes to the complexity of Pakistan's healthcare for the delivery of medical treatment.¹⁸⁻¹⁹ Numerous types of organizations, including the federal and provincial governments, district health authorities, parastatal organizations, social security institutions, non-governmental organizations (NGOs), and private businesses, all contribute to the delivery of health care services.²⁰ The majority of public sector healthcare is provided by the provincial governments while the federal government run vertical, mainly disease-oriented programs. The health care expenditure constitutes 1.4% of country's GDP, with per capital income of US

Despite recent progress, especially the establishment of large private sector hospital and medical universities, the country still does not have the complicated quaternary level of care that is necessary for a successful BMT program. According to the World Health Organization, Pakistan is one of a relatively small number of nations that has a major shortage of health-related human resources. This is due to the fact that there are only around three doctors and one nurse for every 10,000 citizens in the country. Pakistan has high prevalence of inherited blood diseases like thalassemia and bone marrow failure syndromes due to high consanguineous marriages.²¹ For majority of these diseases bone marrow transplant is the only curative treatment.

Gambat Institute of Medical Sciences (GIMS), initially started as a dispensary in the interior of rural Sindh province, has evolved into a large public sector tertiary care institute with well-established solid organ transplant programs. This center has also sub-specialties, advance radiology and oncology services.

ESTABLISHMENT OF BONE MARROW TRANSPLANTATION AT GIMS

The Sindh ministry of health, and the political administration were interested in initiating bone marrow transplant (BMT) facility. Director GIMS, who was the main driving force for this project and involved a senior transplant specialist; who had already established two successful programs in the country. The project was divided into three components; the development of infrastructure, procurement of essential equipment and training of human resource. All the components were initiated simultaneously. A three-storey grey structure, initially constructed for renal transplant was used with essential modifications and converted into BMT unit. The facility consisted of top floor with 18 transplant rooms plus an operation room, first floor 18 rooms for peri-transplant ward and ground floor for OPD and day-care facility. In addition, an adjacent building was used for establishment of hematology, immunology and molecular laboratory. The building had central HVAC system, with laminar flow and HEPA filters for transplant floor. The procurement of equipment was initiated in parallel and it was available by the time of completion of BMT infrastructure. The government of Sindh contributed funding for the endeavor. Three young clinical hematologist, one lab-trained hematologist, an immunologist, paramedics and supporting staff were hired and sent for training to Armed Forces Bone Marrow Transplant Centre Rawalpindi (AFBMTTC), the largest BMT facility in the country and BMT department at Quaid-e-Azam International Hospital Islamabad. A comprehensive three months training program was developed by AFBMTTC administration for each category of staff and the program was closely supervised by the senior consultant. Clinical hematology OPD and indoor service was initiated in January 2021 with continuous supervised hands-on training. Meanwhile selection of suitable BMT patients also began and pre-transplant work-up carried out. First bone marrow transplant procedure was performed on 21 June 2021.

HUMAN RESOURCE CAPACITY BUILDING AND CLINICAL TEAMWORK

Patients undergoing BMT need integrated care by physicians, nurses, and other allied staff plus efficient laboratory support. A twinning with facility for virtual conference was established between BMT facility at GIMS and the senior physician supervising the project located at Islamabad. In addition to distant supervision the supervising physician regularly visited BMT facility at GIMS. The training sessions began in October 2020 and continued until 31st December 2020.

Nursing Staff: BMT nurses are the backbone of any successful program and play critical role in the day-to-day patient management. There are no specialty training programs for nurses in clinical hematology or BMT at GIMS. The need to advance the level of nursing care was a significant challenge in the process of establishing the BMT program. This required enhancing the clinical knowledge base and incorporating nurses into the daily ward rounds. AFBMTC developed a comprehensive curriculum covering all essential aspects of BMT for training of the nurses.

Transfusion Services: An evaluation of the needs was carried out at GIMS by a laboratory trained hematologist, an aphaeresis nurse, and a stem-cell laboratory technician. Based on the results of this assessment, a staged plan was devised to build the fundamental foundations for transfusion services. In addition to the installation of blood irradiator, the essential steps included equipping a stem-cell processing laboratory, procuring an additional aphaeresisequipment for both stem-cell and platelet collections and strategies for availability of blood components were designed, and the staff received the appropriate training. GIMSstaff was assisted by members of the bone marrow processing unit from AFBMTC during the first two collections.

Hematology Diagnostic Laboratory: GIMS personnel were trained for HLA typing, basic molecular diagnoses, Hb electrophoresis and analysis of CD34 counts for calculating stem-cell dose with the flow cytometer. AFBMTC provided training to a lab hematologist, an immunologist, and three technicians.

Pharmacy: The pharmacist from GIMS gained hands-on experience and expertise that were necessary to deliver chemotherapy. The AFBMTC team trained pharmacy personnel in delivering BMT conditioning regimens and leukemia chemotherapy protocols.

Physicians: In the course of their time as clinical observers at the AFBMTC, three clinical hematologists learned different aspects of bone marrow transplant including case selection, pre-transplant workup, BMT conditioning regimens, bone marrow harvesting, stem-cell collections, stem-cell processing and patient monitoring. Incidentally the spouses of three clinical hematologist were also professionals; an immunologist, a gynecologist and a radiologist. It was decided to incorporate gynecologist and the radiologist in the BMT setup in addition to the duties at their parent departments. A thalassemia prevention program with facility for antenatal screening by chorionic villous sampling has been developed at the center. The gynecologist got essential training in fertility preservation and has been tasked to establish pre-transplant fertility preservation setup. The radiologist has been involved for onsite ultrasound and radiological imaging leading to efficient patient care. A three months training for interventional radiology was arranged for the radiologist in parallel to other consultants training. The radiologist has also got training in interventional radiology.

FINANCIAL CONSIDERATIONS

Similar to other public sector services, the operation and long-term sustainability of BMT program depends on government financing. The Government of Sindh provincemade allocations for running this program through annual budget of the institute.

BMT may provide a more cost-effective technique for addressing chronic disorders like thalassemia, the most frequent genetic disease in this area. A patient with thalassemia major will need frequent transfusions and iron chelation therapy as he matures. In low-income countries such as Sri Lanka, Thailand, Bangladesh, and Pakistan, the yearly cost of thalassemia treatment may range from \$1,000 to \$2,500,000. This amount covers hospitalization costs, chelating medications, and blood transfusions. The cost of BMT ranges from \$7000 to \$15000 which is be utilized to treat these individuals, it may be able to reduce

The long-term maintenance expenditures, which, when combined with the societal costs associated with lost productivity, might exceed the original cost of transplantation after ten to twenty years. In contrast to the initial cost of over \$200,000 in industrialized nations, the average cost of comparable procedures in developing countries is between \$10,000 and \$25,000.¹³⁻¹⁷

The initial expenditures for autologous and allogeneic transplants at PAQSJIMS are around \$8,000 and \$10,000 respectively, whereas the Sindh health authority has so far supported 62 transplants.

Due to location in remote area timely backup support for trouble shooting of system faults is difficult to arrange. To overcome this problem local personnel were hired and trained for HVAC, building and equipment maintenance.

INITIAL Challenges

As of July 2023, 62 patients (age range, 4 to 62 years) had undergone allogeneic and autologous transplantations at PAQSJIMS. Diagnoses of the patients was Aplastic Anemia 36; B-Thalassemia Major 12; Fanconi Anemia 3; Acute Myeloid Leukemia 2; Paroxysmal Nocturnal Hemoglobinuria 2; Multiple Myeloma 6; POEM Syndrome 2. Conditioning regimens used in aplastic anemia with reduced intensity while all others had myeloablative conditioning. Day 30 peri-transplant mortality was 30%. The main issues during these transplants were fungal infections occurs in nine patients. We investigated that high rate of fungal infection and it was found to be due construction work being carried out in the surrounding area and moisture in the building resulting from water logging in the soil. Tube wells installed in the vicinity to lower the water table and keep the building dry. More over antifungal spray was incorporated in the routine cleaning and decontamination protocol. Low socio-economic background of the patients and their families also contributed to sub-optimal personal hygiene of the patients. We instituted meticulous patient and family's health education before and during transplant. All these measures were rewarding and has led to improved BMT outcome and reduced peri-transplant mortality. During last 30 transplant our day 30 mortality is <10%

DISCUSSION

The work at PAQSJIMS to establish a large bone marrow transplant facility with adequate infrastructure and human resource development in a remote area was a challenging task but due to persistent efforts of the master trainers plus vibrant administrative support it has become a success story. The experience has shown a number of interesting challenges that may be encountered when establishing such facility in a resource constraint environment especially human resource development and health education of the patients and their families. We recognize that once a program of this kind has been established, it will need persistent efforts to resolve the issues that creep up during the initial phase of functioning. Our experience indicates that one of the most important factors in the success of this program was the twining and coordination with an advanced and large BMT facility; AFBMTC. This center being the well-established and large facility extended support in human resource development and guidance on issues that cropped up during early phase of our functioning. We were able to establish strong partnership with this center that can provided the knowledge, training, and overall direction needed for a complex, multidimensional program. In addition to the twining with an advanced center, there were many defining characteristics of the program's quick development. First, the unflinching support of our medical director who provided leadership and vibrant support for the project, second involvement of an experience person to lead the program and third persistent efforts of master trainers and young BMT physician.

Conclusion

Establishing and successful BMT program in the public sector in resource-limited setting is a difficult task that needs a vibrant administrative support, involvement of experienced person to lead the facility and twining with some advanced center for initial human resource development. Resource constraints nations may have a somewhat higher incidence of complications due to socioeconomic variables and increased infection risks. While transplantation has the ability to satisfy unmet medical needs, future collaborations headed by experienced transplantation facilities will be required for the development and extension of BMT in the poor countries.

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