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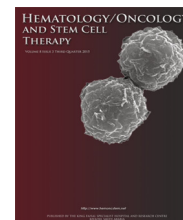
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Cost and quality issues in establishing hematopoietic cell transplant program in developing countries



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Abstract

The hematopoietic cell transplant (HCT) activity has grown significantly over the past two decades in both developing and developed countries. Many challenges arise in establishing new HCT programs in developing countries, due to scarcity of resources and manpower in expertise in HCT. While cost issues can potentially hinder establishment of new HCT programs in certain regions, the focus on quality and value should be included in the general vision of leadership before establishing an HCT program. The main challenge in most developing countries is the lack of trained/qualified personnel, enormous start-up costs for a tertiary care center, and

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quality maintenance. Herein, we discuss the main challenges from a cost and quality perspective which occur at initiation of a new HCT program. We give real world examples of two developing countries that have recently started new HCT programs despite significant financial constraints. We also portray recommendations from the Worldwide Network of Blood and Marrow Transplantation for levels of requirements for a new HCT program. We hope that this review will serve as a general guide for new transplant program leadership with respect to the concerns of balancing high quality with concurrently lowering costs.

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Introduction

Hematopoietic cell transplantation (HCT) is curative for many diseases including hematologic malignancies, bone marrow failure syndromes, primary immunodeficiencies, genetic conditions, hemoglobinopathies, and autoimmune diseases [1]. Due to its curative potential and advances in the supportive care, the mortality of allogeneic transplants has decreased considerably over the past few decades [2], therefore, HCT activity continues to increase exponentially worldwide, including in the developing countries; however, human development index and gross national income per capita are observed to have associations with HCT activity globally [3]. While HCT is potentially curative for many diseases, it is an intensely resource requiring treatment modality which requires adequate capital for start-up costs, and both HCT experts and governmental organizations are looking for guidance for essentials for a new HCT which can be tailored according to the needs of their countries. An HCT program can be established at a reduced cost in a developing country given the financial restraints, but it should have minimum quality standards which should ensure good ethical business principles, as well as have a keen focus on patient safety and a vision of long term sustainability. This paper will focus on two essential aspects of establishment of a new HCT program—quality maintenance and cost reduction strategies; we hope that an analysis of the basic aspects of quality and costs will help the nations without any HCT program to establish HCT activity. Notably, one of the most important aspects of new tertiary care center establishment is lack of expertise (i.e., well trained personnel), however, the detailed discussion of the human resource expertise is beyond the scope of this paper.

Basics of costs and value in healthcare

The definitions in healthcare economics are important and we will review them here first with a description of specific examples in the field of HCT.

Value: How much usefulness or pleasure an individual gets from a commodity or service

Value is still stable and subjective (utility). In the field of HCT, value can be defined by many parameters. Patient reported outcome measures have recently been considered as a new benchmark for HCT survivorship studies [4]. This variable can potentially infer the purest measurement of

value in HCT care. The traditional benchmarks of value in HCT have been considered to be clinical outcomes, for instance, progression free survival, overall survival, etc. However, these outcome based value measures do not contain any input from a patient, thereby, the transplant community is favoring patient reported outcome measures as one of the key measures of success of an HCT and thereby, an important and appropriate proxy for measuring value.

Price/cost

Cost and the (final) price are identical numbers (unless market trends are being analyzed). Real cost should be adjusted for inflation whenever evaluated (e.g., adjusted for 2017 US \$). In the field of HCT, cost measurement analyses have been generally poor, since most of the studies only report the direct costs for a fixed amount of time. Most medical institutions lack transparency when it comes to reporting the actual direct and indirect costs versus charges due to the existing bylaws of their institutions. On average, an allogeneic transplant costs around US\$120,000–400,000 (adjusted to 2012) for the first few months of transplant as reported in literature. For a similar duration of treatments, the costs of allogeneic transplant reported from developing countries are US\$12,500 (unadjusted), US\$17,194 (unadjusted) and US\$31,500 (unadjusted) in Mexico, India, and Brazil respectively [5–7]. Although these cost differences seem huge, with a 10-fold difference in total costs of a procedure, it does not account for important factors which impact clinical outcomes, nor does it impact the “value” parameters from a patient perspective. The average household income and GDP per capita of developing countries is significantly different than the developed countries, thus, in strict economic sense, it may not be appropriate to compare the actual direct cost estimates of countries with each other.

There is a paucity of published data when it comes to the costs of establishing a new HCT center due to many factors. The differences in governmental policies, vendor procedures and the overall goal of establishment of a specialized center (for profit or not-for-profit) are the main determinants which can create considerable variation in the costs incurred in establishing a program.

Competitive market: a marketplace where buyers and sellers are equally informed

Medical business can never be a competitive market, as the buyers (patients) and sellers (physicians) cannot have equal

power of medical decision making. However, joint decision making in all medical aspects including HCT is of utmost importance, given its direct impact on clinical outcomes.

Basics of quality in healthcare

Quality in healthcare is defined as the level of value provided by any healthcare organization or individual, and can be assessed quantitatively or qualitatively. The overall aim of healthcare provision is to utilize medical resources of high quality to all who need them to alleviate the quality of life as well as longevity. Quality measurement in healthcare is the process of using data to evaluate the performance of healthcare institutions, healthcare plans or healthcare providers counter to recognized quality standards.

Measuring the quality of healthcare is an essential step in the process of improving healthcare quality of any specialized program, including HCT. Frequently, when the cost-cutting strategies are employed, they affect the quality of care, which eventually leads to poor and substandard outcomes. Quality measurement can be used to improve an HCT recipient's healthcare by: (1) ensuring multiple check points to patient safety, (2) preventing the overuse, underuse, and misuse of healthcare services, and (3) identifying what works in a particular healthcare setting, e.g., consider endemic factors such as presence of tuberculosis in a country.

Cost-control in HCT

For controlling costs of a specialized healthcare program, it is necessary to firstly focus on minimal requirements for adequate and sustainable functioning of the program. The requirements have three levels as recommended by the Worldwide Network for Blood and Marrow Transplantation (WBMT) workshop (Table 1). Measures such as isolation capacities, when added up at macroeconomic level, can tremendously increase the annual initial costs of transplant programs, however, the net benefit of such measures is clearly demonstrated by improvement in survival due to reduction in fatal invasive infections, as well as low transmission of nosocomial microbes. The costs associated with

a single outbreak of a hospital acquired infection, e.g., methicillin-resistant *Staphylococcus aureus* or clostridium difficile infections, can drive up the indirect and direct costs of a program to astounding levels. Thus, it is preferred as a Level I WBMT recommendation to have isolation facilities in an HCT center. The Level II requirements are a preferred obligation of a committed HCT center, and can help in reduction of many HCT-related complications of an HCT program. A classic consideration would be a high-efficiency particulate air (HEPA) filter which can reduce the risk of many infections, particularly tuberculosis, which can be rapidly fatal in immunocompromised patients.

Level III indications for setting up an HCT unit include optimal tertiary care facilities and state of the art outpatient and inpatient facilities with HEPA filters. These are not mandatory requirements for starting up an HCT unit, however, the eventual goal of institutional leadership should be towards acquiring Level III care provision essentials.

An important aspect for establishment of a new HCT program to be considered along with initial capital is sustainability costs, particularly for quality maintenance. Let us take the example of HEPA filters. There is an initial cost of instalment of each unit for these filters, then there are maintenance costs, air conditioning systems and electricity costs; lastly, there may be costs associated with inspection and certification of HEPA filters. Manpower, training of ancillary and core staff, establishing standard operating procedures, and lean processes for each avenue of a new program also add tremendous costs to a new unit.

Like many industries in which the risks of sustainability are great, an HCT unit establishment should be a very well thought out decision, preferably with some input (or direct involvement) with the governmental agencies, especially in developing countries. The essential questions in establishment are provided in Table 2, the most important of which are the exact needs, capital, leadership, and capacity. All the essential questions need to be answered before embarking on HCT center establishment. A key aspect is the number of beds allocated for HCT recipients, as the initial costs in setting up a tertiary care unit may range from few thousand US\$ per bed to more than a million US\$ per bed, depending on a number of factors.

Table 1 Worldwide Network for Blood and Marrow Transplantation (WBMT) levels of care for establishment of hematopoietic cell transplant (HCT) center.

	Level I Minimum	Level II Preferred	Level III Ideal
Inpatient unit	Clean single bedded rooms with isolation capability	HEPA filtered positive pressure rooms preferably with ante-room (s)	Standalone HEPA filtered unit with positive pressure rooms
Outpatient clinic	Single patient examination rooms		HEPA filtered unit with day infusion unit
Intensive care unit		ICU with positive/negative pressure isolation rooms and ventilator support	Level III ICU with capabilities for hemodialysis/Continuous Venovenous Hemofiltration/ Extracorporeal membrane oxygenation

HEPA = high-efficiency particulate air; ICU = intensive care unit.

Table 2 Costs and quality essentials in establishing a hematopoietic cell transplant (HCT) center.

	Description	Availability and challenges	Potential solutions
Needs	Exact needs of HCT should be assessed, e.g., most prevalent indications of HCT in a country; demographic analysis; economic analysis	Inaccuracy of data; incomplete data; absence of guidance in assessing needs and developing feasibility reports	Thorough needs assessments by transplant community along with referring specialists. Obtaining accurate epidemiologic data with the help of governmental or nongovernmental organizations. Professional consultations with management consultancy firms if affordable
Capital needed	Assessment of exact monetary amount needed for startup and sustainability costs. Number of inpatient beds is one of most important long term drivers of both direct and indirect costs given the specialized bed units needed for HCT	Quality assessments and quality improvement programs may not be routinely incorporated in initial capital costs. All aspects not accounted for initially (e.g., hospital engineering for positive pressure ventilated rooms; HLA typing facilities; optimum blood bank facility, etc.) Cost-utility and cost-benefit analyses for most of the clinical management aspects are lacking	Quality checklists for hospital management to be included in initial capital. Start up HCT program priorities should be well defined with input from multiple experts both within and outside the institution (e.g., whether to start up with allogeneic vs. autologous HCT program; to start up with matched sibling donor program first but should have a clear plan for next step in near future for next donor source, e.g., unrelated donor, cords or haplos)
Leadership and expertise	HCT is a highly specialized field, and for startup programs should have experienced personnel well trained in this field. Applies to physicians, nurses, technicians, and all other allied health staff	Lack of HCT expertise. Hematologists without adequate HCT training or expertise are frequently available in most of the developing countries. However, for initiation of a new HCT program, experienced and well trained transplant physicians and nurses are essential for the program's success	Focus on human resources in acquiring adequate well trained and experienced staff with expertise in HCT. This applies to both nursing and physician work force.
Quality and sustainability	Quality of a program consists of many avenues: (1) Quality of patient care (includes safety) (2) Quality control procedures of laboratory (3) Value determinants as proxy for quality of a program, e.g., clinical outcomes, PROMs	Maintaining quality of an HCT program requires additional human resource services for staffing, information technology tools, error monitoring, and damage control programs which can lead to higher costs	For sustainability of a new HCT program, the leadership, entrepreneurs (and/or venture capitalists) and governmental authorities should be convinced that focus on quality is essential in HCT given the high stakes of this tertiary care service. WBMT recommendations should be taken into account for the planning of a start-up program. "Twinning" or "pairing" strategies should be utilized for continuous advice over a period of years (e.g., 5 year contract/Memorandum of Understanding) with experienced HCT programs in other countries Compliance measurement tools should ideally be automated to prevent errors which can translate into huge cost-savings

<p>Accreditation</p> <p>Data has indicated that acquiring international standards for accreditation by HCT related organizations can directly impact (and improve) clinical outcomes. At least 2 accreditation bodies exist that should have a necessary relationship with HCT programs</p> <ol style="list-style-type: none"> (1) Stem cell standards (2) Blood bank standards 	<p>It is expensive to set up a new program in a resource constrained country which will fulfill all the standards for an HCT program</p> <p>Both FACT-JACIE and blood bank accreditation organizations (e.g., AABB) have minimal requirements and optimal requirements for accreditations. It is not necessary to fulfill all requirements for initiation of an HCT program; however, the ultimate vision should be towards accreditation within a few years of the first transplantation. In order to plan for accreditation, it would be worthwhile (even 2–3 years ahead of time) to get direct advice from FACT or JACIE to work on getting standard policies and procedures in place.</p>
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FACT = Foundation for the Accreditation of Cellular Therapy; JACIE = Joint Accreditation Committee-ISCT & EBMT; PROM = patient reported outcome measures; WBMT = Worldwide Network for Blood and Marrow Transplantation.

If needs assessment is incomplete or inaccurate, then professional consultancy groups, which are the management consulting firms, should be involved for advice, preferably with those firms who have experience in preparing comprehensive data reports for business in developing countries. This initial investment in management companies to have an accurate feasibility report for establishing a tertiary care center may actually be cost-saving in the long run, and moreover, they can continue to provide professional advice on many management aspects, e.g., experience curves and business matrices, which can help in hospital administration.

Quality control in HCT

Delineation of quality control (QC) and quality improvement (QI) measures should be an essential requirement of HCT programs in order to improve outcomes. The QC principles should be thoroughly documented in the hospital policies and measurement of compliance itself should be monitored at well-defined intervals. One of the goals of HCT programs should be eventual recognition by international societies which provide accreditation to the HCT program. The two large professional societies providing guidance for accreditation and eventual certification include Joint Accreditation Committee-International Society for Cellular Therapy & European Society for Blood and Marrow Transplantation (JACIE) and the Foundation for the Accreditation of Cellular Therapy (FACT). Together, both societies/organizations have assimilated the international standards for HCT programs which give guidance to HCT programs in all clinical and technical matters [8].

Quite often, the question arises as to whether having an internationally accredited program impacts on the outcomes of an HCT program or not. Recent data suggests that obtaining accreditation via JACIE compared to not having any international accreditation results in a superior relapse-free survival (hazard ratio 0.85; 0.75–0.95) and overall survival (hazard ratio 0.86; 0.76–0.98) in allogeneic transplant recipients [9]. Thus, it is advisable that one of the planning aims of HCT programs should be towards acquiring FACT-JACIE standards, with the eventual goal of obtaining, and then maintaining certification. It is understood that this would not be possible for a start-up program; however, planning to obtain FACT-JACIE certification takes years and is an important aspect for both patient safety and for maintaining quality of an HCT program.

Costs versus quality for a new HCT program

The relationship of costs and quality in a healthcare setting is very complex, as an abundance of variables which define value and quality play a role. Although the notion that reduction of costs is inversely proportional to the quality performance and QC, it may not be true in the long run when it comes to sustainability. Since a “low cost and high quality” model is considered to be a Utopian phenomenon, the leadership charged with development of a new program should prioritize the avenues which require utmost capital, while keeping an eye on QC.

Recent (21st century) examples of new HCT center establishment in developing countries include Nigeria and Bangladesh, both of which have vastly distinct models of HCT [10,11]. The annual GDP per capita (nominal) of both the countries is under US\$3000; moreover, the human development index ranking of both countries is one of the lowest globally, denoting extremely limited financial and social resources. Lastly, the strategic priorities of fund allocation are vastly different in different regions of the globe. Nigeria initiated an allogeneic program first by transplanting a pediatric patient with sickle cell disease (SCD), while a Bangladesh program initiated the HCT unit by performing an autologous HCT for an adult myeloma patient. While these two approaches are widely different with respect to the capital investments, risks of the procedure, age of the recipient, and the indication for transplant, they exemplify the practical real world issues in the HCT unit establishment paradigm. Both programs at initiation had different reasons for a start-up program for allogeneic versus autologous HCT, e.g., in Nigeria, 2–3% of the population has SCD and since no efficient national blood bank services exist, many patients with SCD die early due to complications of SCD; thus, it was appropriate for the Nigerians to think of establishing an allogeneic program despite the costs associated with it, given the needs assessment of that country. Bangladesh, by contrast, had ample support from the federal government as well as from the Massachusetts General Hospital to provide expertise at every level, including engineering of the HCT unit, training the nursing staff, and above all, constant guidance and availability on clinical aspects of transplantation. Thus, they were justified in starting up an autologous HCT program first, and future planning towards starting allogeneic transplants.

In addition to governmental and institutional support, nongovernmental organizations have also been proven to help to establish HCT centers in developing countries. The Cure2Children foundation is such a nongovernmental organization which has helped to initiate HCT for children with thalassemia in India and Pakistan, while maintaining low direct costs for an average cost of US\$10,000 (Consumer Price Index unadjusted) per HCT [7]. Additionally, many countries which are in the process of setting up a new HCT center have partnered with other countries with well-established experienced HCT centers, to lower the costs and to improve the quality of the HCT program, a concept well-known in the field of healthcare as “twinning”.

Thus it all depends on the needs, eventual goals, and resources when deciding on the balance for quality versus costs for a start-up HCT program. Once the plan of establishing an HCT center is finalized based on needs assessment, then the charter of the center should include the basic aspects of value in healthcare which affect both costs and quality, as depicted in Table 2.

Conclusions

There is an inarguable need for the establishment of HCT centers in countries where the diseases for which HCT is the only cure are endemic. In order to establish a new HCT center, the vision of the leadership and the institutional charters should include policies which place emphasis

on QC and QI in the long run. To lower the cost by compromising quality will negate the purpose of HCT, since the outcomes will be affected adversely. Minimal requirements of a new HCT program should include the Level I recommendations by the WBMT. The eventual goal of a newly established HCT program should be to improve quality and provide value from an individual, institutional, and societal perspectives.

Conflicts of interest

There are no conflicts of interest to disclose from any authors.

Authors' contributions

Shahrukh Hashmi wrote the first draft. All authors contributed substantially to the conception, acquisition, analysis, and interpretation of the data for the work and approved the final approval of the version to be published.

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