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REVIEW

Stem cell transplantation in India

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This paper outlines the BMT activity in India and describes in some detail the transplant program at the Christian Medical College, Vellore. In September 2005, data from six transplant centers in India were collected and a total of 1540 transplants have been performed in a country of over one billion population. At the center in Vellore, from October 1986 to December 2006, a total of 626 transplants have been performed in 595 patients, with 28 patients having more than one transplant. Thalassemia accounted for a third of these transplants: the country has over 20 million carriers and 10 000 children are born each year with thalassemia major. The average cost of allogeneic BMT in India is around $15 000–20 000, and this is considerably lower than the cost in the West. India needs to develop more transplant centers with adequately trained personnel, as there is great need for them. Improvements in the economy mean that more patients can afford this treatment.
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Introduction

India has a population of over one billion people with about 5% being able to afford the very best treatment, 25% in the middle class with increasing income and 70% who cannot afford a transplant unless it is provided by the state, and this is not likely considering other urgent health priorities.[1] With 20 million carriers for thalassemia and 10 000 children being born with thalassemia major each year, if one-third of these patients have an HLA-matched sibling donor, there is a potential to cure 3000 children with BMT.[2] If one considers six per million as the incidence of aplastic anemia, there would be 6000 new cases/year, and if 10% of these patients are suitable candidates for transplant, then the country would need to do 600 transplants per year for this disease alone. India's gross domestic product (GDP) per capita in 1999 was $370 and in 2006, this had risen to $3460 (source: World Population Data Sheet 1999/2006). This means that many patients can now afford to have a transplant even if resources are not available from the state or private insurance.

The process of collecting information and maintaining a database of transplant activity in India has not been streamlined. In September 2005, data were collected from six transplant centers in the country and their location is given in Figure 1.

HLA typing

The first prerequisite for an allogeneic BMT program is HLA typing: this is available in tertiary hospitals and private laboratories. Serology is still performed for AB (HLA class I typing of AB antigens) typing, but most laboratories use DNA methods for DR (HLA class II typing of DR antigens) typing. The Asian Indian Donor Marrow Registry (AIDMR) is located in New Delhi with a BM database of 3000 donors. High-resolution typing is available at the AIDMR, but only one unrelated transplant using cord blood from the NMDP has been performed so far. There are a few private cord blood banks in India.

Transplant unit

Many hospitals in the West perform transplants in standard single rooms. The much higher level of antimicrobial resistance and poor quality of the environment in developing countries make it prudent to have a dedicated HEPA-filtered transplant unit where there is a high level of control of the environment.

BMT data from India

In September 2005, data were collected from six transplant centers in India and a total of 1540 transplants have been performed in India at these centers (Table 1). Of these, half were autologous transplants mainly for myeloma. As further national data are not available, the rest of this paper gives data on transplant activity at the Christian Medical College, Vellore.

Transplant program at Vellore

Figure 2 shows the number of transplants performed and the type and Figure 3 indicates the proportion of allogeneic

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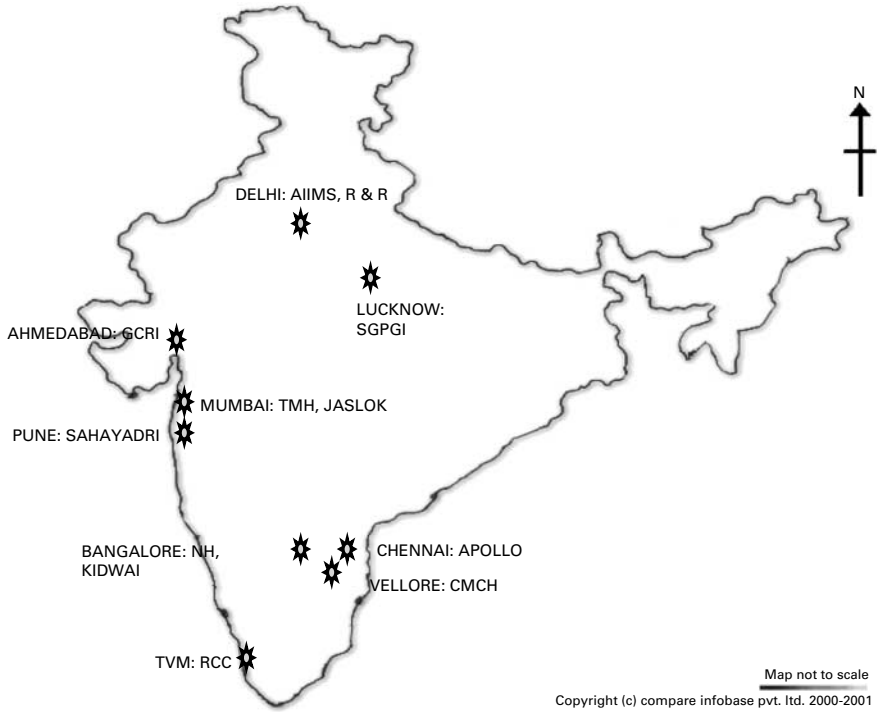

Figure 1 Major BMT centers in India (2005).

Table 1 Transplant activity in India (September 2005)

	Autologous	*Allogeneic*	*Total*
Christian Medical College Hospital, Vellore	117	522	639
Tata Memorial Hospital, Mumbai	90	178	268
All India Institute of Medical Sciences, New Delhi	144	66	210
Apollo Hospital, Chennai			159
Jaslok Hospital, Mumbai	49	19	70
Research and Referral Hospital of the Armed Forces, New Delhi	26	37	63
Sahayadri Hospital, Pune	7	59	66
Gujarat Cancer Research Center, Ahmedabad	32	0	32
Sanjay Gandhi Post Graduate Institute, Lucknow			25
Kidwai Memorial Hospital, Bangalore	3	0	3

transplants performed for thalassemia in relation to the other diseases. Table 2 gives the distribution of diseases for which a transplant has been performed.

Conditioning

For thalassemia, conditioning has been performed with various combinations of BU and CY with or without antilymphocyte globulin. Conditioning for leukemia has been performed with the Tutschka protocol of BU 16 mg/kg and CY 120 mg/kg. For aplastic anemia, we now use mainly fludarabine-based conditioning[3] and CY TBI is used for ALL.

GVHD

CYA and short MTX are the main protocol for GVHD with a target CYA level of 250 ng/ml.

Antimicrobial policies

Acyclovir is administered at a dose of 15 mg/kg/day i.v. starting day +1, is switched to oral dose after day 14 and is continued for 2–3 months. Most patients and donors are CMV IgG-positive and ganciclovir is started when the CMV-PCR becomes positive post transplant. Trimethoprim sulfa and penicillin are given for 1-year post transplant.

Tuberculosis

Records of 217 BMT patients during the period 1986–1999 were reviewed and mycobacterial infections were diagnosed in three patients, (1.38%), all of whom presented with extrapulmonary disease, and two of these patients had disseminated disease.[4] Infection with *Mycobacterium tuberculosis* is not a common problem in allogeneic BM recipients even in an endemic area, but when it occurs, it is

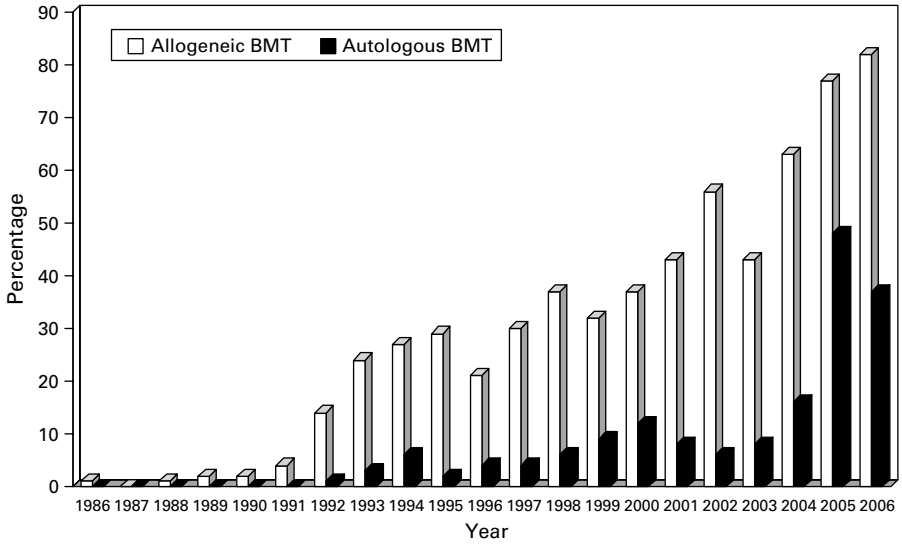

Figure 2 BMT at Christian Medical College Hospital, Vellore (October 1986–December 2006).

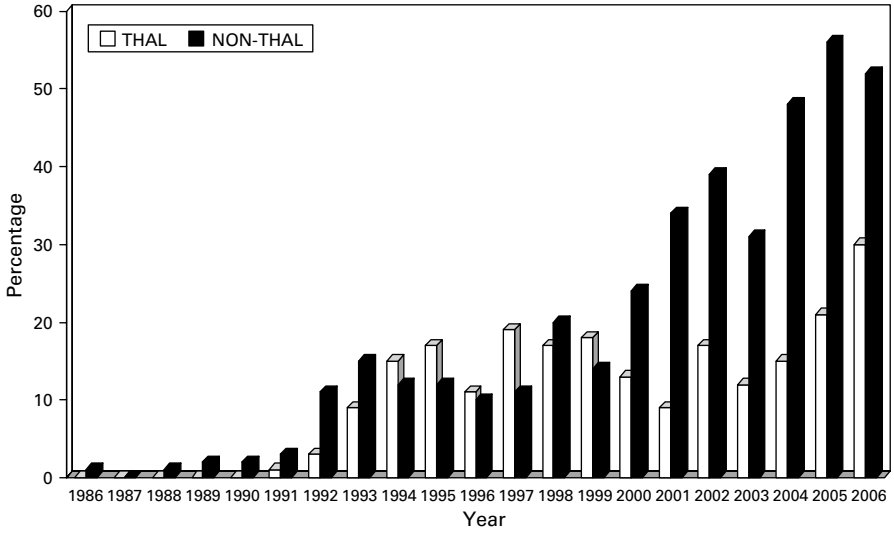

Figure 3 BMT at for thalassemia, compared with other indications. Christian Medical College Hospital, Vellore (October 1986–December 2006).

Table 2 Indications for BMT—Christian Medical College Hospital, Vellore (October 1986–December 2006)

Diseases	*Patients*	*Transplants*	*BMT-1*	*BMT-2*	*BMT-3*
Thalassemia	218	227	218	9	—
AML	107	111	107	4	—
ALL	39	39	39	—	—
CML	91	99	91	7	1
Aplastic anemia	84	90	84	5	1
Fanconis anemia	8	10	8	1	1
Myelodysplasia	29	31	29	2	—
Miscellaneous	19	19	19	—	—
Total	595	626	595	28	3

usually disseminated with predominantly extrapulmonary involvement. On the basis of these data, we do not use isonicotinic acid hydrazide prophylaxis, as it will complicate the interpretation of abnormal liver function tests post transplant.

Other infections

There were 415 documented infections among 304 transplants: bacterial (34.9%), viral (42.9%), fungal (15.9%) and other infections (6.3%), including tuberculosis.[5] Bacterial pathogens were mainly Gram-negative bacteria (80%) as compared with Gram-positive (20%) bacteria. The common Gram-negative bacteria were nonfermenting Gram-negative bacteria (24.9%), *Pseudomonas* (17.9%), *Escherichia coli* (17.9%) and *Klebsiella* (9.7%). The major source of positive cultures was blood (53.7%) followed by urine (25.5%) and sputum (8.9%). In all, 133 of 304 (43.7%) transplants had 178 documented viral infections. The common viral infections were due to cytomegalovirus, herpes group of viruses and transfusion-

Table 3 Outcome of allogenic BMT for thalassemia Christian Medical College Hospital, Vellore (5-year Kaplan–Meier estimate of overall survival and EFS)

Class	*Number*	*Survival (%)*	*EFS (%)*	*Rejection (%)*
All patients	218	72.3 ± 3.1	65.3 ± 3.3	14.6
Class I	15	71.8 ± 11.98	71.8 ± 11.98	0
Class II	89	82.6 ± 4.1	78.3 ± 4.4	12.4
Class III	114	64.5 ± 4.6	54.6 ± 4.8	18.4

related hepatitis; 60 of 304 (19.7%) transplants had 66 documented fungal infections. Common fungi included *Aspergillus* species (69.7%), *Candida* (22.2%) and *Zygomycetes* (8.1%).

BM harvest. For all thalassemia transplants, BM is the stem cell source and we use sternal aspiration needles, which result in little postoperative pain. For leukemia and aplastic anemia, G-CSF-mobilized PBSC are preferred.

Chimerism
Engraftment and chimerism are documented with an amylogenin PCR for sex-mismatched transplants and a panel of short tandem repeats (STRs) and variable number of tandem repeats (VNTRs). Gene scan is used for quantification.[6]

BMT for thalassemia

From October 1991 to December 2006, 218 patients with thalassemia were treated with an allogeneic BM transplant: patients were risk-stratified by the criteria proposed by Lucarelli: class I: 15 (6. 9%), class II: 78 (35.8%) and class III: 125 (57.4%), and this is a reflection of the poor pre-transplant care that these patients receive. With a mean follow-up of 133 months (range: 6–183), 72 (80.8%) 89 children in class II are alive and well, free of transfusion and of immunosuppression (Table 3). However, among the 114 patients who were in class III, there was a 34.4% mortality and 19.4% rejection, which means that these patients should receive better pre-transplant care and should be taken early for BMT. Allogeneic BMT at $15 000–20 000 is equivalent to the cost of 3 years of transfusion and chelation and is a good alternative in the developing world.

Allo-SCT in India costs around US$ 15 000–20 000, and this is considerably lower than the cost in the West. It therefore makes sense for the country to develop more transplant centers, and with worldwide medical tourism on the increase, India can (after providing for its own citizens) be on the map for BMT.[7,8]

Data on all transplants at Christian Medical College Hospital, Vellore are being reported to the CIBMTR.

Research activity revolves mainly around pharmacokinetics of BU and CY and conditioning regimens for thalassemia.[9,10]

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Conflict of interest

Dr Chandy has received consulting fees from Astra Zeneca and is in receipt of a grant from the Department of Biotechnology, Government of India.

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