Original Articles

Allogeneic haematopoietic stem cell transplantation: The Army hospital experience

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ABSTRACT

Background. We analysed the results of allogeneic haematopoietic stem cell transplantation (HSCT) in various genetic disorders, bone marrow failures and haematological malignancies done from 2002 to 2010 at the Army Hospital, Research and Referral, Delhi.

Methods. A total of 119 matched-related allogeneic-HSCTs (allo-HSCTs) were done in 114 patients (men 76, women 38) aged between 2 and 60 years. Peripheral blood stem cells (n=75) and bone marrow (n=43) were used as the source of stem cells.

Results. The overall survival was 62.3% (71/114) at a median follow-up of 34 months. Graft versus host disease (GVHD) was seen in 42 (36.8%) patients; grade III/IV acute GVHD in 17 (15%) and chronic GVHD in 24 (21%) patients. There were 4 (3.5%) graft rejections and one non-engraftment. The overall mortality was 37.7% (n=43) and the main causes of death were GVHD (32%), infections (26%), relapse (23%) and regimen-related toxicity (11%).

Conclusion. Our results are comparable to published data in most disease conditions. With improvements in GVHD prophylaxis and better supportive care, we need to further reduce our mortality and morbidity.

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INTRODUCTION

Haematopoietic stem cell transplantation (HSCT) has revolutionized the treatment of numerous haematological disorders, considered incurable in the past.1,2 While the technique is well established in developed countries, it is evolving in developing countries. Some of the constraints relate to the lack of trained personnel, the cost and the need for multidisciplinary support.3 Hence, there is an imbalance in supply and demand. In India, the first HSCT was done in 1983 and till December 2008, a total of 1757 allogeneic HSCTs (allo-HSCTs) had been done.

Our centre is a tertiary care referral centre for over a hundred armed forces hospitals spread over India providing free treatment to armed forces personnel and their families. We have an HSCT programme and have been doing about 35 HSCTs every year.4 We report our experience with allo-HSCTs.

METHODS

Patients

Patients, aged 2–60 years with a diagnosis of thalassaemia major, aplastic anaemia (including Fanconi anaemia), acute and chronic leukaemia, myelodysplastic syndrome (MDS), paroxysmal nocturnal haemoglobinuria (PNH) and congenital dyserythropoietic anaemia (CDA) were considered for allo-HSCT. Selected patients underwent human leucocyte antigen (HLA) matching with related donors (siblings and parents). All patients who had a 6/6 HLA matched donor were further evaluated for left ventricular ejection fraction by echocardiography, pulmonary function test and any overt or occult focus of infection especially in the ear, nose, throat or oral cavity.

All patients who underwent allo-HSCT for thalassaemia major were risk stratified using Lucarelli criteria, which propose three classes based on evidence of good iron chelation, hepatomegaly and presence of portal fibrosis on liver biopsy. Class I were patients with good iron chelation, no hepatomegaly and non portal fibrosis. The presence of one or two factors was classified as class II and presence of all three factors as class III.

HLA matching

All patients underwent molecular typing using sequence-specific primers (SSP), which is a low-resolution DNA-based typing for HLA using polymerase chain reaction (PCR). HLA loci A, B and DR were matched in all patients. The donors were matched siblings in all except one instance where the mother was the donor.

Donor screening

All donors were screened for any underlying disease including cytomegalovirus (CMV), hepatitis B virus (HBV), hepatitis C virus (HCV) and herpes virus by PCR. They were also screened for malaria and syphilis.
Transplant protocol

Venous access. A double lumen Hickman broviac catheter was inserted under general anaesthesia in children and under local anaesthesia in adults. Each central catheter remained in situ for 1–3 months.

Conditioning. All patients were administered chemotherapy-based conditioning. Busulphan (Bu) and cyclophosphamide (Cy) regimen, as proposed by Tutschka et al., in a total dose of 16 mg/kg over 4 days and 120 mg/kg over 2 days, respectively, were given to patients with leukaemia and MDS. The conditioning for thalassaemia included injection ATGAM (equine antithymocyte globulin [ATG]) in a dose of 90 mg/kg over 3 days in addition to Bu–Cy as mentioned above. In non-myeloablative transplants done for aplastic anaemia, an intensive short-term immunosuppression with fludarabine and ATG with low-dose oral busulphan were used.6,7

Stem cell source. Peripheral blood stem cells (PBSCs) were harvested using a cell separator. Bone marrow, harvested from the posterior superior iliac spine using Jamshidi bone marrow aspiration needles, under general anaesthesia, was collected into a blood bag containing citrate phosphate dextrose adenine solution without using a filter. The donor was administered 25 units/kg of unfractionated heparin intravenously before commencing the bone marrow harvest. A minimum nucleated cell dose of 3x10^8/kg recipient weight was aimed at and harvest volume was calculated accordingly. In the initial 20 cases, the cell dose was also corroborated with CD34 counts and once concordance between the dose of mononuclear cells (MNC) and CD34 was established, subsequent transplants were done using the adequacy of dose of MNC. In most haematological malignancies and bone marrow failure syndromes PBSC was used, while in child donors only bone marrow was harvested (as PBSC harvest was not feasible). The donor was informed about the merits and demerits of bone marrow versus PBSC, and allowed to make a choice, whenever possible.

Total parenteral nutrition (TPN). It was given to patients when oral intake was compromised because of mucositis. We used, ready-to-use commercially available TPN. In adults, 1026 ml was infused through the central catheter which provided 900 kcal in 24 hours. In children, a paediatric formulation was used. No TPN filters were used. Trace elements (copper, iron, iodine, manganese, selenium, zinc and molybdenum) were administered separately. TPN was discontinued once the patient started taking oral fluids. The average duration for TPN was 10–14 days.

Blood component therapy. All cellular blood products were irradiated (25 Gy per bag) before transfusion. Single donor platelets were harvested using a cell separator. Standard practices were followed in providing blood component support for all major, minor and bidirectional ABO-incompatible transplants. The preferred ABO-type of platelet in major and minor ABO-incompatible transplants was of donor and recipient type, respectively. Plasma-depleted platelet component of donor ABO type was used in bidirectional transplants. Other ABO types were infused in the absence of the preferred ABO types.8,9

Preventive therapy. Prophylaxis for graft versus host disease (GVHD) in most instances consisted of cyclosporine (CSA)/methotrexate (MTX) while mycophenolate mofetil/tacrolimus was used in case of CSA intolerance. Intravenous (i.v.) CSA from day 3 was administered daily till mucositis settled and oral fluids were tolerated, following which oral CSA was started (usually double the dose of i.v. CSA). On the diagnosis of acute GVHD, all patients were given i.v. methyl prednisolone 2 mg/kg body weight per day for a minimum of 7 days followed by tapering of steroids in case of regression of GVHD and addition of other immunosuppressive agents (mycophenolate, tacrolimus, ATGAM or monoclonal antibodies) for grade III/IV disease.

Prevention of haemorrhagic cystitis secondary to use of high-dose cyclophosphamide was done by giving a continuous infusion of 2-mercaptoethanesulphonic acid sodium salt (MESNA) starting 12 hours before and continuing till 12 hours post-cessation of cyclophosphamide along with hydration.

Antimicrobials. None of the patients received any gut sterilization with oral quinolones. Oral fluconazole was used as antifungal prophylaxis in the initial transplants. However, we noticed that colonization by non-Candida albicans species occurred in these patients. Therefore, fluconazole prophylaxis was discontinued. As all our patients were seropositive for CMV, i.v. ganciclovir was given for prophylaxis against CMV starting on day –10 and continued till day –2 in a dose of 5 mg/kg daily; i.v. acyclovir, 5 mg/kg every 8 hours was started on day 1 and continued till the patient started oral feeds when a switch to oral acyclovir was made. This was continued till immunosuppressives were used, and longer if GVHD occurred.4

An algorithm was used to manage febrile neutropenia based on microbial sensitivity. Usually, a third generation cephalosporin with anti-pseudomonal spectrum and an aminoglycoside was the initial therapy followed by addition of anti-staphylococcal (vancomycin or teicoplanin) and antifungal agents if fever persisted. A high index of suspicion for fungal infections was kept and antifungal therapy was instituted early with voriconazole or amphotericin.

Response and toxicity assessment

Patients were assessed, twice a day, for any adverse event due to the preparative regimen with monitoring of complete blood counts, liver and renal function tests, serum electrolytes and blood glucose. Every 2 weeks samples were sent for CMV DNA, HBV DNA and HCV RNA. To assess engraftment and degree of chimerism, patients were monitored at regular intervals (days 30, 60 and 100) by donor- and host-specific DNA markers; by variable number tandem repeats (VNTR). Neutrophil engraftment was defined as the first day of absolute neutrophil count (ANC) >500/µL and platelet engraftment as the first day of unsupported platelet count >20 000/µL.

We allowed one person (usually a family member) to stay with the patient during this labour-intensive procedure. This provided moral and physical support to the patient, especially children, who were in isolation for 3–4 weeks. Only pressure cooked food, prepared in a common kitchen in the transplant unit, and filtered, boiled water was used by patients.

All transplants were done in a high efficiency particulate air (HEPA) filtered unit. Patients were shifted to a dedicated air conditioned, non-HEPA filtered, step-down unit, once neutrophil engraftment occurred. All patients after discharge were followed up in the outpatient department every week for the first 3 months and subsequently every month for one year or till stoppage of immunosuppressive therapy, whichever, was later.

Statistical analysis

The data were censored for this study on 31 March 2011, so that the minimum follow-up data are of 11 months. Response was assessed by evaluating the overall survival for non-malignant diseases and disease-free survival for malignant diseases; documenting acute and chronic GVHD, and any other adverse
events. Survival was estimated using the Kaplan–Meier method at the median of the follow-up period. All p values were derived from likelihood ratio statistics and were one-sided.

RESULTS

A total of 119 transplants were done in 114 patients (Table I) with a median age of 17 (2–60) years, 38 of whom were women. PBSCs were used in 75 (63%) transplants, bone marrow in 43 (36%) and bone marrow with cord blood in 1. Forty-nine patients (43%) were below 18 years of age.

The overall survival was 62.2% at a median follow-up of 34 months. Acute GVHD occurred in 34 patients (30%), of whom 17 had grade III/IV acute GVHD. Chronic GVHD was seen in 24 patients (21%), of whom 11 had extensive chronic GVHD (Table II). There were 4 (3.5%) graft rejections and one non-engraftment. The difference in the incidence of acute GVHD between bone marrow and PBSC (6.98% v. 18.42%) groups was not significant (p=0.14). However, chronic GVHD was significantly higher (p=0.006) in the PBSC group (bone marrow 7% v. PBSC 30.7%).

Of the 43 patients (37.7%) who died, 37 died within one year and 6 between one and two years after transplant. The major causes of death were GVHD (14, 32%), infections (11, 26%), relapse (10, 23%) and regimen-related toxicity (5, 11%).

Acute myeloid leukaemia (AML)

Of the 30 patients with AML who had an HSCT, 25 were in complete remission 1 (CR1), 4 in CR2 and 1 patient who underwent a second transplant was in CR3. Grade III/IV acute GVHD occurred in 3 (10%) and chronic GVHD in 5 (16%) patients, 3 of whom had extensive chronic GVHD (2 skin and liver, 1 lung). Fourteen (47%) patients were alive and disease-free at a median follow-up of 25.5 (11–59) months (Fig. 1). Sixteen (53%) patients died including 6 following a relapse (4 of CR1; 1 of CR2 and 1 of CR 3), 6 of pneumonia with sepsis, 2 with veno-occlusive disease (VOD), 1 of grade III/IV acute GVHD and 1 due to chronic lung GVHD.

Acute lymphatic leukaemia (ALL)

Thirteen patients underwent HSCT, of which 8 were in CR1 (including 3 Philadelphia chromosome+ [Ph+]) and 5 were in CR2. Seven (54%) patients were alive and disease-free at a median follow-up of 50 (12–99) months (Fig. 1). Grade III acute GVHD was seen in 2 patients and chronic GVHD in 4 (31%) patients (2 limited, 2 extensive). Of 6 (46.2%) patients who died, 2 died due to grade III acute GVHD; 1 due to extensive chronic GVHD and 3 due to relapse (2 of CR2 and 1 of CR1 with Ph+ disease).

Chronic myeloid leukaemia (CML)

All patients were in CML-chronic phase 1 (CP1) and of the 19 patients, 13 (68.4%) are alive and disease-free at a median follow-up of 59 (11–95) months while 6 (32.6%) patients died (Fig. 1). Grades III/IV acute GVHD was seen in 4 (20%) patients and chronic GVHD in 8 (40%) patients, of which 3 had extensive chronic GVHD (1 skin and liver, 2 lungs). One patient transplanted using PBSC developed grade II acute skin GVHD which was successfully treated with CSA and a short course of steroids. One year post-HSCT, this patient developed significant weight loss, extensive oral ulcers and severe cholestatic jaundice. Skin and mucosal biopsy confirmed chronic GVHD. The liver biopsy revealed portal fibrosis with lymphocytic infiltration. There was loss of bile ducts with cholestasis consistent with a diagnosis of vanishing bile duct syndrome. This patient died due to severe chronic GVHD. The other causes of death were VOD in 1

Table I. Characteristics of patients undergoing haematopoietic stem cell transplantation

<table>
<thead>
<tr>
<th>Item</th>
<th>Acute myeloid leukaemia (n=30)</th>
<th>Acute lymphoid leukaemia (n=13)</th>
<th>Chronic myeloid leukaemia (n=19)</th>
<th>Aplastic anaemia (n=16)</th>
<th>Thalassaemia major (n=26)</th>
<th>Miscellaneous (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age (years)</td>
<td>24 (5–54)</td>
<td>19 (9–32)</td>
<td>27.5 (7–46)</td>
<td>22 (12–46)</td>
<td>6 (2.5–13)</td>
<td>16 (2–60)</td>
</tr>
<tr>
<td>Median follow-up (months)</td>
<td>58 (11–84)</td>
<td>51 (13–92)</td>
<td>59 (11–95)</td>
<td>16 (12–56)</td>
<td>35 (11–92)</td>
<td>42 (12–58)</td>
</tr>
<tr>
<td>Source of stem cells</td>
<td>BM, PB 28</td>
<td>BM, PB 21</td>
<td>BM, PB 14</td>
<td>PB 15, BM 1</td>
<td>BM 26, BM 4, PB 5, BM+PB 1</td>
<td>BM+PB 1</td>
</tr>
<tr>
<td>Median cell dose (MNC×10⁹/kg)</td>
<td>7 (2.33–9.2)</td>
<td>6.4 (1.9–7.5)</td>
<td>5 (2.5–8.2)</td>
<td>6.75 (3.1–7.7)</td>
<td>5.3 (2.2–9.7)</td>
<td>5.2 (2.9–8.6)</td>
</tr>
</tbody>
</table>

Values in parentheses are range

BM bone marrow  PB peripheral blood  CB cord blood  MNC mononuclear cells

Table II. Outcomes of allogeneic haematopoietic stem cell transplants

<table>
<thead>
<tr>
<th>Item</th>
<th>Acute myeloid leukaemia (n=30)</th>
<th>Acute lymphoid leukaemia (n=13)</th>
<th>Chronic myeloid leukaemia (n=19)</th>
<th>Aplastic anaemia (n=16)</th>
<th>Thalassaemia major (n=26)</th>
<th>Miscellaneous (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median neutrophil engraftment (days)</td>
<td>12.3 (8–32)</td>
<td>11 (9–14)</td>
<td>11.3 (9–14)</td>
<td>8.5 (5–12)</td>
<td>13.8 (9–13)</td>
<td>12.6 (7–20)</td>
</tr>
<tr>
<td>Median platelet engraftment (days)</td>
<td>14 (10–40)</td>
<td>13.6 (9–36)</td>
<td>14.5 (10–33)</td>
<td>12.9 (7–19)</td>
<td>18.2 (8–34)</td>
<td>18.5 (10–46)</td>
</tr>
<tr>
<td>Acute grade III/IV GVHD (n=17), site</td>
<td>3</td>
<td>2</td>
<td>4</td>
<td>1</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Chronic GVHD (n=24)</td>
<td>5</td>
<td>4</td>
<td>8</td>
<td>3</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Severe VOD (n=15)</td>
<td>4</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Infections (%)</td>
<td>26 (86)</td>
<td>12 (92)</td>
<td>16 (84)</td>
<td>12 (75)</td>
<td>17 (65)</td>
<td>8 (80)</td>
</tr>
<tr>
<td>Mortality (%) (n=43)</td>
<td>16 (53.3)</td>
<td>6 (46.2)</td>
<td>6 (31.6)</td>
<td>5 (31.3)</td>
<td>6 (23.1)</td>
<td>4 (40)</td>
</tr>
</tbody>
</table>

GVHD graft versus host disease  VOD veno-occlusive disease  Ext. extensive  Ltd. limited
patient, grades III/IV acute GVHD in 2; sepsicaemia in 1 and relapse in 1 patient.

**Thalassaemia major**

Of the 26 patients who underwent allo-HSCT in our series, 4 belonged to class I, 14 to class II and 8 to class III (Table III). The only patient who underwent cord blood transplant rejected the graft but was successfully transplanted a second time, using bone marrow from the same sibling. The overall survival of patients was 76.9% (20/26) at a median follow-up of 35 (11–92) months (Fig. 2).

**Acquired severe aplastic anaemia**

Of 16 patients in this group, 11 (68.8%) are alive and disease-free at a median follow-up of 16 (11–56) months. Only 4 (26.5%) patients had GVHD including 1 acute GVHD (grade III/IV) and 3 chronic GVHD (1 limited and 2 extensive). Five (31.3%) patients died; 3 due to sepsis, 1 due to extensive chronic GVHD and 1 due to massive pericardial effusion with cardiac arrhythmia (Fig. 2).

**Miscellaneous**

Three patients with Fanconi anaemia had HSCT. One developed graft rejection while two developed acute GVHD, one of whom went on to develop extensive chronic skin GVHD. The patient with graft rejection was successfully transplanted a second time using the same donor. In juvenile myelomonocytic leukaemia, of the 2 patients, both infants, one relapsed and died 5 months after the transplant and the second is alive and disease-free at 51 months of follow-up. In MDS, of the two patients, both developed acute GVHD and one of them went on to develop chronic GVHD of the lung with sepsicaemia and succumbed to these complications, 11 months after transplant. One patient with PNH developed grade III/IV acute GVHD and died 5 months after bone marrow transplant. Two patients with congenital pure red cell aplasia (PRCA) were transplanted, of whom one also had Duchenne muscular dystrophy (DMD). The child with DMD is transfusion-free and has not had any deterioration in his muscle power 45 months post-HSCT. The other patient with PRCA developed mild-VOD and haemorrhagic cystitis, which responded to conservative treatment and is disease-free 4 years post-transplant.

**Infections**

We documented 130 infections including 79 (61%) bacterial, 32 (24%) viral, 18 (14%) fungal and 1 parasitic infection. Ninety-one (79.8%) patients developed at least one episode of fever with temperatures of 38.3 °C or above. Twenty-six patients (23.3%) developed a second episode of fever. The median duration of fever was 8 (range of 3–85) days. Sixty-nine of the initial febrile episodes (75.5%) occurred in the neutropenic phase. There were no localizing features of infection in 70 (92%) of the second febrile episodes were in the neutropenic phase, and 24 (92%) of the second febrile episodes were in the neutropenic phase. There were no localized features of infection in 70 patients (77%), whereas the infection was localized to the lungs in 11, gastrointestinal tract in 6, skin and soft tissues in 3, and head and neck in 1. There was no difference between patients transplanted for malignant and non-malignant indications or in myeloablative versus non-myeloablative HSCTs.

**Bacterial infections.** There were 79 documented bacterial infections, 42 (53%) occurred in the first 30 days post-HSCT. Gram-negative bacteria (GNB) were isolated in 61 (77%) and Gram-positive bacteria (GPB) in 18 (14%) cultures. The common GNB isolated included *E. coli* (48%), *P. aeruginosa* (13%), non-fermentative GNB (12%), *Enterobacter* (2%) and *K. pneumonia* (2%). The GPB were *Staphylococcus aureus* (13%) and coagulase-negative *Staphylococcus* (8%). Positive bacterial cultures were obtained from the blood (65%) followed by urine (12%), sputum (8%) and catheter-related infections (5%). There were no infections with tuberculosis.
Viral infections. Thirty-two viral infections were reported post-HSCT, including 16 CMV (50%), 6 HCV (19%), 4 herpes simplex virus 1 and 2 (13%), 3 HBV and herpes zoster each (9%).

Fungal infections. There were 18 documented fungal infections and the common fungi identified were Candida spp. (10, 55%), Aspergillus spp. (6, 33%) and zygomycetes (2, 10%). For infections due to Aspergillus, all patients fulfilled the Centers for Disease Control (CDC) criteria of either proven or possible fungal infection. The majority of infections were seen in the first 100 days post-HSCT and the most common site was the lung (9, 50%). The other sites included the central nervous system, paranasal sinuses, gastrointestinal tract, skin, catheter-related, isolation from blood (Candida) and disseminated forms.

Parasitic infections. Only 1 patient was seropositive for toxoplasma post-HSCT. There were no infections with malaria.

Non-myeloablative transplants
Twenty-six patients had 27 non-myeloablative transplants. VOD occurred in 2 patients, acute and chronic GVHD in 5 and infections in 9 patients. Twelve patients died (46%), including 4 due to GVHD, 5 due to relapse, and 1 each due to severe sepsis and multiorgan failure, pneumonia and renal failure, and pneumonia alone. The nadir ANC was <100/μl in both the myeloablative and non-myeloablative transplants, though the median neutrophil engraftment of 10 days in the non-myeloablative group was shorter than the 12.4 days in the myeloablative group. The overall survival in the non-myeloablative group was 56% (15 patients) at a median follow-up of 26 months.

Graft rejection and non-engraftment
Graft rejection occurred in 4 patients (AML 2, Fanconia anaemia 1 and thalassaemia 1). Both patients with AML had a second transplant but died subsequently—1 of relapse after 5 months and 1 of septicaemia. The patient with thalassaemia is alive but requires transfusion support. The patient with Fanconia anaemia, who had a second transplant from the same donor, successfully, is stable and disease-free. One non-engraftment occurred in a patient with CML.

GVHD
Acute GVHD was observed in 34 (30%) patients and of these 17 had grade III/IV acute GVHD. Chronic GVHD was seen in 24 (21%) patients of whom 11 had extensive chronic GVHD. Of 17 patients with acute grade III/IV GVHD, 1 patient had isolated grade III/IV gut involvement, 1 had grade II/IV liver disease and 4 patients had isolated skin involvement. The other 11 patients with acute GVHD had more than one system involvement, including 5 with involvement of the gut, liver and skin simultaneously. Nine patients died due to acute GVHD (grade III/IV) and 4 due to extensive chronic GVHD.

Regimen-related toxicity
Hepatic VOD occurred in 15 (12%) transplants, of which 4 (3.6%) were fatal. Two of the fatal VODs were in patients with thalassaemia with severe iron overload pre-transplant. One patient with aplastic anaemia succumbed to pericardial effusion with tamponade. Two patients developed haemorrhagic cystitis and were managed with hydration and bladder irrigation with satisfactory recovery.

Non-HEPA setting
Eighteen allo-HSCTs done in single air conditioned rooms of the general haematology ward, a non-HEPA setting, from May 1998 to December 2001, and have not been included in the present analysis. These data have been compared with the 114 patients who underwent allo-HSCTs in a HEPA filtered setting in this study (Fig. 3). These included 10 patients who had CML, 4 AML, 2 ALL, 1 CLL and 1 thalassaemia major. The median age was 26.5 (4.5–39) years and the median dose of cells administered was 6.1×10^6 MNC/kg (range 1.7–15). Acute GVHD was seen in 9 (50%) and chronic GVHD in 3 (16%) patients. Of these 18 transplants, 8 (44%) are disease-free at a median follow-up of 10.5 years. Ten (56%) patients died; 3 of grade III/IV acute GVHD, 3 of extensive chronic GVHD, 3 of sepsis and 1 of VOD and pneumonia.

DISCUSSION
The overall survival in the HEPA filter setting has been superior to non-HEPA filter setting (65% v. 44%), though not significant (p=0.138), presumably due to the disparity in patient numbers in the two groups. Considering environmental conditions, with high incidence of antimicrobial resistance in developing countries, we recommend HEPA filtered units for allo-HSCTs, despite the feasibility of doing the transplant in clean rooms.12

The incidence of acute GVHD between bone marrow and PBSC (6.98% v. 18.42%) groups was not statistically significant (p=0.142). However, chronic GVHD was significantly higher (p=0.0058) in the PBSC group (bone marrow 7% v. PBSC 30.7%). Similar findings have been observed by other workers.

In thalassaemia major, our results are comparable with those of Pessaro, Italy and the Christian Medical College, Vellore, Tamil Nadu.13,14 These centres have the largest series of thalassaemia major transplants in the West and India, respectively. A high mortality rate in class 1 emphasizes the unpredictability of sepsis and regimen-related toxicity in HSCT.14

The overall survival of 68.8% for severe aplastic anaemia is comparable to published results from India and elsewhere.15,16 Most of our patients were diagnosed early and minimally transfused given the network of more than 100 armed forces hospitals spread all over India. A delay in diagnosis and multiple transfusions pre-transplant, negatively impact transplant outcomes in this group of patients.
The disease-free survival in patients with leukaemia was between 46.6% and 68.4% at a median follow-up of 25.5 months which is comparable to other published data from India and the West. Although, imatinib mesylate has replaced allo-HSCT as first-line therapy for CML, with long-term molecular responses, HSCT remains the only curative treatment for CML. If done within 1 year of diagnosis, especially in younger patients (<30 years), sibling-related allo-HSCT may be a superior and cost-effective treatment option in developing countries. The American Society of Hematology panel has reported 50% leukaemia-free survival on a 5-year follow-up and a 25% incidence of relapse on an 18-year follow-up in patients with CML. Hence, a long-term, close follow-up is warranted with BCR–ABL monitoring for molecular relapse and early intervention with donor lymphocyte infusion or imatinib mesylate. The European Bone Marrow Transplant Registry (EBMTR) has reported a 10-year survival in 65%–70% of children. Early diagnosis followed by transplant within 1 year has contributed largely to our excellent results in CML–CP.

Three patients with Fanconi anaemia and 2 with congenital PRCA are disease-free at a median follow-up of 42 and 48 months, respectively. One patient with PRCA and DMD (a fatal form of muscular dystrophy) also underwent transplant primarily for transfusion-dependent PRCA. The patient had a static clinical course over the past 4 years, post-transplant. Muscle biopsy has also shown 8%–10.4% donor cells on DNA typing with 100% donor chimerism in the blood.

The cost of an allo-HSCT in private hospitals in India is about ₹10–12 lakh (US$ 20–24 000). In contrast, our patients, in the armed forces, were treated free of cost. An allo-HSCT in the West can cost US$1 500 000–400 000. This vast difference in cost opens up a vast scope for medical tourism.

Over the past 12 years, the transplant programme has helped us evolve and improve our practice. The change from serological HLA typing to molecular typing has reduced the incidence of GVHD. Better facilities in our blood bank to ensure round the clock availability of platelet support has helped us reduce the threshold for prophylactic platelet transfusion to below 20 000/µL. Improvement in microbiology services (including introduction of Galactomannan assay) has made our antimicrobial cover more effective. The change from serological HLA typing to molecular typing has reduced the incidence of GVHD. Better facilities in our blood bank to ensure round the clock availability of platelet support has helped us reduce the threshold for prophylactic platelet transfusion to below 20 000/µL. Improvement in microbiology services (including introduction of Galactomannan assay) has made our antimicrobial cover more effective.

The cumulative results at our centre have been comparable to the published data from India and the West. In the Armed Forces, healthcare is a priority and all efforts are made to ensure delivery of ‘the recommended ‘standard of care’. This coupled with an excellent tracking system ensures a near 100% follow-up, helping us achieve good outcomes.

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