Autologus Hematopoietic Stem Cell Transplant: Horizon 2020

Raut SS1 and Shah SA2

1Consultant Medical Oncologist, HCG-Ranchi, Ex Resident Doctor AI Gujarat Cancer And Research Institute, Ahmedabad, India
2Unit Head Of Bone Marrow Transplant And Associate Professor, Gujarat Cancer Research Institute, India

Abstract

Autologous stem cell transplant (ASCT) has evolved over last 5 decades a lot. There are enormous advances in the technique right from mobilization, collection, counting of stem cells to preservation, conditioning and peritransplant care. By the end of this decade we feel necessity to explore the scope and update the details and minutes of ASCT particularly in oncology grossly as well as disease-wise. We delineate the basics of the procedure and advances till date. Also we aimed to summarise the implementation of these advances in India by analyzing the data and information in published articles. This may further help physicians to understand the complex procedure with simplicity and may guide the research workers and authors as reference tool.

Keywords: Autologous stem cell transplant; ASCT; Cancer; India

Introduction

Hematopoetic stem cell transplant (HSCT) is exponentially growing in India [1-4]. Cheaper cost is the main reason behind this rise. There are 3 types of HSCT according to the source of stem cells viz. autologous stem cell transplant (ASCT) where the source is oneself, allogenic stem cell transplant (Allo SCT) where the source is different person and syngenic stem cell transplant where the source is identical twin.

High dose chemotherapy (HDCT) and radiotherapy (RT) is used to ablate the bone marrow producing a fatal marrow aplasia, which is salvaged by ASCT. ASCT also helps to decrease the tumour cell burden to the minimal, thus giving a prolonged progression free survival (PFS). ASCT does not involve long term immunosuppression or delayed immune reconstitution. Elderly age was a limitation to access of allogenic transplant, which lead to invention of ASCT. Table 1 shows gross difference between ASCT and Allo SCT.

Hematopoetic stem cells (HPSC)

These are CD34 expressing cells present in spongy bone marrow (0.5-1%) [e.g. pelvic bones, ribs, skull, spine] and in circulating blood (0.05%-0.1%) [1-4]. These also express human leukocyte antigen (HLA) antigens, but lack blood group antigens. They have the capacity of engraftment and differentiation into erythrocytes, leukocytes and platelets.

Phases of ASCT: ASCT includes various processes like Collection, Cryopreservation, HDCT, Thawing, stem cell infusion and Supportive care.

Limitations: ASCT is discouraged in those with Karnofsky score <70, LVEF <40%, Compromised FEV1, DLCO<40% of predicted normal, Creatinine >3 mg/dl, heavily pretreated patients, and Chemorefractory patients. Table 2 shows checklist for pretransplant workup before posting any patient for ASCT.

Counseling: Family meeting before HSCT is necessary to counsel and educate regarding role of relatives accompanying inside the bone marrow transplant room and those visiting from outside. Counseling also be done for fertility preservation and sperm banking. Half of the patients undergoing ASCT are those having multiple myeloma. Table 3 shows the prevalent indications of ASCT in clinical practice.

Insertion of catheter: A double lumen catheter (DLC) is inserted in jugular or subclavien vein under local anesthesia. This serves both for purpose of collection and intravenous access for stem cell transplantation. The catheter placement is confirmed by chest x-ray and the insertion site is maintained clean and dry with regular change of dressings along with flushing. Catheter care may require analgesics, and training to inform signs of infection like fever, redness, swelling, drainage, increased tenderness. Catheter is removed after the HSCT at the time of discharge.

Collection

Hematopoetic stem cells (HPSC) for ASCT can be collected either from bone marrow (BM) or peripheral blood (PBSC). They are viable for 5 to 7 days at 2 to 4°C. For long term preservation, they can be preserved in a balanced salt solution with cryoprotectant (e.g. DMSO, dimethyl sulfoxide) in liquid nitrogen. Bone marrow (BM) collection for stem cells usually should have the volume about 10 to 15 ml/kg patient weight (1000 ml approx). Table 4 shows the required quantity and preservation techniques of stem cells during ASCT.

Mobilization

HPSC are mobilized either with filgrastim (cytokine only) on outpatient basis or low dose cyclophosphamide (chemo mobilization) [1-4]. Filgrastim may cause bone pains and require analgesics, plenty of liquids and rest. Low dose chemotherapy (cyclophosphamide) based mobilisation requires antiemetics and mesna for bladder protection. One need to be aware of cytotoxicity of mesna also which manifests as cytopenia, fever, chills, cough, hematuria.

Plerixafor recently used works through disrupting the bond of chemoreceptor type 4 and stromal derived factor-1-alpha, thus moving progenitor cells to peripheral blood. In heavily pretreated patients where cytokine only based mobilization is insufficient, chemotherapy or plerixafor based mobilizations may be preferred. Apheresis may be...
Eating the chemotherapy and/or radiation. The goal of conditioning is to destroy stem cell infusion as “Zero”. The preparatory regimen may consist of hospitalization.

Ancestim (Recombinant human stem cell factor) is a soluble surface molecule on bone marrow stromal cells which is used in conjunction with filgrastim. The doses of mobilizing agents are described in Table 5.

### Hospitalization

Patient is hospitalized usually 2 days to one week before transplant. The countdown of the days starts considering the day of stem cell infusion as “Zero”. The preparatory regimen may consist of chemotherapy and/or radiation. The goal of conditioning is to destroy the cancer cells. Healthy bone marrow also undergoes the subsequent destruction. The type and amount of chemotherapy depends on the disease. Side effects of chemotherapy should be well explained before. Eating normally as long as the patient can is encouraged. Personal hygiene should be educated. Light physical activity may be allowed to sleep better and assists cardiac activity and muscle circulation.

Approximately 3 weeks of hospitalization is required for ASCT as compared to four to five weeks for Allo SCT. The setup is usually a HEPA filter unit with private bathrooms for patient use only. It may contain television, telephone to feel as homely as possible. All things are explained in Table 6.

### Conditioning

Most commonly used conditioning regimens for various cancers are as follows: for multiple myeloma single agent melphalan, for lymphoma BEAM (BCNU, etoposide, Ara C, Melphalan) and CBV (cyclophosphamide, BCNU, etoposide), for AML BuCy (Busulphan, Cyclophosphamide) or BuMel (busulfan, Melphalan) or BEA (busulfan, etoposide, Ara –C) and for germ cell tumour TICE (Paclitaxel, Ifosfamide, Carboplatin, Etoposide). There are a number of short term as well as long term side effects linked with high dose chemotherapy. Short term side effects are explained in Table 6.
Complications of ASCT

On the day of transplant, infusion reactions like fever, chills, hypotension, chest pain, cough can occur. They are managed like usual blood transfusion reactions.

During engraftment process, bacterial, viral and fungal infections usually pertaining to prolonged grade 4 neutropenia occur. Other side effects of HDCT are nausea, vomiting, fluid electrolyte imbalance, mucositis, malnutrition, bleeding, blood transfusion support, hepatic venoocclusive disease, acute respiratory distress syndrome.

Long term complications are relapse of cancer, leukemia, myelodysplasia, interstitial pneumonitis and hemorrhagic cystitis.

Cytopenia recovers within 3 weeks, the duration of which can be decreased by 4 days with filgrastim. Packed red cells (PRBC) and platelet transfusion (SDP preferably) and other supportive care is required same as management of grade 4 neutropenia. Irradiating all the blood products before transfusion reduces the transfusion associated GVHD. Stem cells never to be irradiated.

Major infections which are gram negative bacteria, gram positive bacteria, clostridia, herpes and fungi are treated with antibiotics, antivirals, antifungals, growth factors. Hepatic veno-occlusive disease (tender hepatomegaly, jaundice and fluid retention in first 2 to 3 weeks) and idiopathic pneumonia syndrome, acute respiratory distress (ARDS) are infrequent but not to be missed. Table 7 explains the infection prophylaxis.

Transplant related mortality (TRM) should be minimal (usually <3%). Relapses are commoner in ASCT than allo-SCT. Table 8 enlists causes of death in ASCT.

Side effects of radiation are short term (e.g fatigue, skin redness, dryness, fever, nausea, vomiting, diarrhoea, mucositis and headache) and long term (e.g skin cancer, xeroderma, xerosis of mouth, cataracts, pneumonitis).

Chemotherapy can be associated with sterility. Sperm banking or fertilized ova preservation should be advised.

Stem Cell Transplantation (SCT) Proper

Stem cell infusion is same as blood transfusion. Premedication and antiallergics should be used. Mannitol and diuretics can be used when hemolysis is suspected after stem cell transfusion. The day of stem cell infusion is labelled as day “Zero”. Transfusion reactions are managed as same as blood transfusion. Patient may experience the garlic like odour for some time which is due to the preservatives.

Engraftment day is usually marked by first of 3 consecutive days with absolute neutrophil count (ANC) >0.5 x 10^9/L and unsupported platelet count >20 x 10^9/L on 3 consecutive days. Engraftment occurs in 2 weeks with PBSC and in 3 weeks with bone marrow stem cells. Filgrastim reduces duration of severe neutropenia by 2 to 4 days. Blood counts are monitored with daily CBC. There is increased risk of infection with decreased absolute neutrophil count (ANC) below 1000/cmm. This is tide over with supportive antibiotics. Hand washing is critical in asepsis. Anemia is associated with fatigue and thrombocytopenia manifests with bruising, bleeding. Blood component support is required to maintain Hb >8 g% and platelet >10,000 cmm. Irradiation and Leukocyte-reduced products should be used for prevention of HLA immunization. Severe mucositis impairs feeding and should be managed with total parental nutrition (TPN).

Discharge advice

Discharge advice consists of complete diet, personal hygiene, home care explanation which includes cleanliness of patients atmosphere, and avoiding crowded places or sick people. These precautions are recommended till immune reconstitution which takes about 3 months after ASCT. After discharge there is frequent follow up for blood investigations and clinical assessment for signs or symptoms of infection. Post-transplant clinic visits are generally scheduled one to three times a week. Patients are informed to report if fever, chills, catheter problems if catheter is in situ, hematuria, dysuria, chicken pox exposure, diarrhoea, nausea, vomiting, malena, bleeding gums. Outside food should be avoided. Animal contact including pets and birds should be avoided. Travel, public toilets, restaurants, strenuous activities should be avoided. Sex is allowed if platelet and total leukocyte counts are normal and there are no sexually transmissible infections in any of the partners. Barriers such as condom are recommended.
during immunocompromised period. Table 9 lists important points in discharge advice.

**Multiple Myeloma (MM)**

Stem cells are viable at 2 to 4°C for 5 to 7 days, hence ASCT in MM can be done without use of DMSO [5-24].

Triple drug induction (including novel drugs), early upfront ASCT and maintenance therapy are standard of care in all transplant candidates of myeloma. The dose of melphalan may vary according to age of patient. Tandem ASCT are useful only in those patients who are not in VGPR at the time of first ASCT. ASCT remains useful even in relapse setting as salvage, in patients with renal dysfunction and even in novel agent era. High risk biology e.g. t(4;14), del(17p) or high β2 microglobin have poor prognosis even with ASCT. Though the OS benefit remains controversial, there is definite evidence of CR and EFS benefits. Also, transplant outcomes are better with early ASCT than late ASCT. Pet scan and minimal residual disease (MRD) are increasingly used to enhance ASCT outcomes. Table 10 describes ASCT strategies in myeloma.

**Lymphoid malignancies**

Relapsed Hodgkin and relapsed, aggressive non Hodgkin lymphoma (NHL) demonstrate 40%-55% cure rate with ASCT [25-33]. ASCT is controversial in indolent NHL and T-cell NHL. CBV, BEAM and TBI based regimens are most commonly used conditioning regimens for lymphoma. TBI free conditioning have lower TRM. Chemotherapy or plerixafor based mobilization should be considered in heavily pretreated cases.

**Follicular lymphoma (FL), first remission (CR1):** The routine use of first line ASCT consolidation in FL is not advisable in the rituximab era. Though ASCT can give more EFS/PFS, it doesn’t translate into more overall survival. Also, ASCT is associated with increased TRM and higher number of secondary malignancies (GITMO 2008).

**Follicular lymphoma (FL), relapsed:** Chemosensitive FL patients (CR2) undergoing ASCT achieve long term remissions irrespective of rituximab but its status is controversial due to better outcomes of salvage chemotherapy. ASCT may be occasionally preferred over allo-SCT due to its acceptability and well known security profile. ASCT is best reserved for chemo sensitive, relapsed FL patients who are not candidates for allo-SCT. CIBMTR-2004 retrospective data predicts better OS and EFS with purged ASCT (62% vs. 55%).

**Transformed FL:** ASCT is recommended for transformed FL with non-bulky and chemo sensitive disease.

**Mantle cell lymphoma (MCL):** Upfront consolidative ASCT in CR1 is standard of care in MCL and 5 year survival with ASCT is 60-70%. ASCT is also recommended for chemo sensitive, relapsed MCL patients, who are not candidates for allo-SCT where 5 year survival is 44%. Hermine et al (2012) demonstrated near doubled EFS (84 months vs. 49 months) with marked OS advantage with R-DHAP induction ASCT. Rituximab and addition of cytarabine in induction improved the OS. However mantle cell leukemia should be treated with allo-SCT.

**Waldenstrom macroglobulinemia (WM):** ASCT should be considered in relapsed chemosensitive WM patients who have received 2 or 3 different therapies, 5 year PFS and OS being 40% and 68% respectively.

**Marginal zone lymphoma (MZL):** In relapsed, chemosensitive MZL, ASCT should be considered though the data is very scant.

**Chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL):** ASCT is not helpful in CLL/SLL.

**Diffuse large B cell lymphoma (DLBCL), first remission:** ASCT is not indicated in first line in DLBCL due to very good outcomes of chemo immunotherapy but in double hit lymphoma treated with RCHOP it is recommended.

**DLBCL, relapsed disease:** ASCT is standard treatment for relapsed, chemosensitive DLBCL. CORAL study (2010) established the role of ASCT (EFS 53%) for relapsed DLBCL after RICE/ RDHAP salvage regimens [23].

**Burkitt lymphoma (BL):** ASCT is not required in BL in first CR due to curative chemo immunotherapy. In relapsed chemosensitive BL, ASCT gives 3 year PFS of 30%.

**Hodgkin lymphoma (HL), relapsed or primary refractory:** ASCT seems curative and standard therapy in relapsed chemosensitive HL as well as primary refractory HL. CIBMTR (2001, 1999) data shows that patients in CR2 have better prognosis and 40% of primary refractory patients can be benefited by ASCT[22].

**T cell lymphoma (TCL):** ASCT is recommended in T cell NHL as upfront consolidation except in ALK positive anaplastic large cell lymphoma. ASCT is also preferred for relapsed, chemo sensitive TCL patients (CR2) who are not candidates for allo-SCT.

### Table 9: Discharge advice.

| Complete diet plan
| Personal hygiene
| Follow up schedule and discharge medicines
| Catheter care if catheter in situ
| Barrier sex
| Avoiding crowds
| Signs of infection and emergency contact numbers
| Preventive care like avoiding smoking and tobacco |

### Table 10: ASCT strategies in MM [5-24].

<table>
<thead>
<tr>
<th>Strategies</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Upfront consolidative ASCT</td>
<td>EFS benefit</td>
</tr>
<tr>
<td>Young fit patients (200 mg/m² melphalan)</td>
<td>OS benefit</td>
</tr>
<tr>
<td>Elderly patients (100-140 mg/m² melphalan)</td>
<td>OS benefit</td>
</tr>
<tr>
<td>2. Tandem ASCT</td>
<td>For those who are in VGPR at the time of first ASCT No OS benefit</td>
</tr>
<tr>
<td>Tandem (delayed second) ASCT for those who are not in VGPR at the time of first ASCT</td>
<td>EFS and OS benefit</td>
</tr>
<tr>
<td>3. ASCT on relapse/Salvage ASCT/Second ASCT</td>
<td>OS benefit</td>
</tr>
<tr>
<td>4. ASCT with advanced renal failure (140 mg/m² melphalan)</td>
<td>OS benefit</td>
</tr>
<tr>
<td>5. ASCT in the era of novel agents with triplet induction</td>
<td>EFS benefit</td>
</tr>
<tr>
<td>6. Lenalidomide/ Bortezomib maintenance replaces thalidomide maintenance</td>
<td>OS benefit, 25% risk reduction in mortality but threefold increase in second malignancies</td>
</tr>
<tr>
<td>7. Oral ixazomib maintenance -2 years</td>
<td>PFS benefit</td>
</tr>
<tr>
<td>8. MRD after ASCT</td>
<td>Predictor of EFS</td>
</tr>
<tr>
<td>9. PET CT after ASCT</td>
<td>Predictor of EFS</td>
</tr>
<tr>
<td>10. Plerixafor in mobilization</td>
<td>Post heavy chemotherapy mobilization</td>
</tr>
<tr>
<td>11. Propylene glycol free formulation of Melphalan</td>
<td>Higher bioavailability</td>
</tr>
</tbody>
</table>
Post-transplant maintenance therapies for lymphoma: Rituiximab maintenance has shown to increase OS in MCL but not in FL or DLBCL. Also brentuximab is approved for post ASCT consolidation and maintenance in high risk HL.

PET scan in ASCT: PET negative state before and after ASCT predict improved ASCT outcomes.

Rarer plasma cell dyscrasias: HDCT with melphalan has been effective in Light chain amyloidosis, ligh chain deposition disease and POEMS syndrome but randomized clinical trials are not available.

Acute myeloid leukemia (AML)

Patients of AML with favorable and intermediate risk cytogenics can be considered for ASCT after induction therapy if suitable donor is not available [34].

Acute lymphoblastic leukemia (ALL)

Routine ASCT in ALL in first line as consolidation or maintenance or in relapsed patients is not recommended [35]. Some older studies have demonstrated similar EFS with ASCT as compared to allo-SCT in selected patients. However Philadelphia chromosome positive patients receiving tyrosine kinase inhibitors (TKI) with chemotherapy can be considered for ASCT when suitable donors are not available. ASCT is an option when allograft donor is not available.

Germ cell tumour (GCT)

ASCT is potentially curative in high risk GCT relapsed after or refractory to first line chemotherapy regimens [36]. Carboplatin and etoposide are used in conditioning of GCT. Table 11 highlights role of ASCT in non-myeloma cancers at present.

Late complications of ASCT: ASCT reduces life expectancy as compared to healthy population and there is increased risk for opportunistic infections, iron overload, endocrine disturbances, osteoporosis and second malignancies. Table 12 describes monitoring for late complications of ASCT.

Preventive maintenance after transplant: One should follow healthy practices i.e. abstaining tobacco and alcohol, having healthy foods, exercise and regular sunscreen use. Blood tests—Annual CBC, biochemistry, blood glucose level, serum lipid levels, thyroid hormone levels.

ASCT can increase the risk of secondary cancers e.g. skin cancer, head and neck cancer, breast cancer, thyroid cancer (papillary thyroid carcinoma), and brain cancers (astrocytomas). The risk of hepatocellular carcinoma (HCC) is increased in patients having hepatitis C infection.

Indian Scenario

‘Indian Stem Cell Transplant Registry (ISCTR)’, a nonprofit organization established in 2004 compiles and maintains the database of HSCT activities in various centres in India. By 2020 there will be near 100 centres carrying out HSCT in India [37-65]. Though the population of India is several times more than USA, the HSCT activity in India is 10 times less than USA. This is the failure to deliver standard of care curative treatment strategies in cancer. By 2020, India may cross 20,000 transplants. Out of these grossly 60% estimated to be allo-SCT, the rest 40% being ASCT. Half of all ASCT are generally MM, followed by mature B cell NHL and HL.

ASCT costs 4 to 7 lakh in India and the cost is 20 times more in developed nations. Hence, India has a good potential for medical tourism in HSCT especially for Middle East countries and South Asian countries.

Gram negative organisms dominate in cultures in India, as compared to gram positive organisms in western countries. A few reports from India show good outcome of HSCT even in compromised infrastructure e.g. without HEPA filters. Worldwide, the trend of “ASCT with bone marrow proper” collection has been shifted to “peripheral blood stem cell based ASCT” with comparable efficacy.

<table>
<thead>
<tr>
<th>1</th>
<th>Follicular lymphoma</th>
<th>First remission</th>
<th>Not recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Mantle cell lymphoma</td>
<td>First remission</td>
<td>Standard</td>
</tr>
<tr>
<td>3</td>
<td>Waldenstrom macroglobulinemia</td>
<td>First remission</td>
<td>No data</td>
</tr>
<tr>
<td>4</td>
<td>Marginal zone lymphoma</td>
<td>First remission</td>
<td>Not recommended</td>
</tr>
<tr>
<td>5</td>
<td>SLL</td>
<td>Relapsed</td>
<td>Only in chemosensitive</td>
</tr>
<tr>
<td>6</td>
<td>DLBCL</td>
<td>First remission</td>
<td>Recommended in double-hit DLBCL treated with RCHOP.</td>
</tr>
<tr>
<td>7</td>
<td>BURKITT lymphoma</td>
<td>First remission</td>
<td>Not recommended</td>
</tr>
<tr>
<td>8</td>
<td>Hodgkin lymphoma</td>
<td>Relapsed</td>
<td>Standard of care</td>
</tr>
<tr>
<td>9</td>
<td>T cell lymphoma</td>
<td>Primary refractory</td>
<td>Standard of care</td>
</tr>
<tr>
<td>10</td>
<td>AML</td>
<td>First CR</td>
<td>Favourable and intermediate cytogenetic risk</td>
</tr>
<tr>
<td>11</td>
<td>ALL</td>
<td>When allograft donor not available.</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>Germ cell tumour</td>
<td>First remission</td>
<td>Not recommended</td>
</tr>
</tbody>
</table>

Table 11: Strategy of ASCT in malignancies other than myeloma and recommendations [24-36].
Early referrals should be encouraged along with development of infrastructure (Table 13).

Conclusion

By 2020 India is projected to a growth about 9 billion dollars in medical tourism. India is preferred medical hub even by UK, Russia and USA due to low cost of treatment. South Asian and Middle East countries prefer Indian healthcare due to poor infrastructure in respective countries and close proximity to India. Chennai, Kolkata, Mumbai, Hyderabad, and Delhi-NCR are popular destinations for treatment for patients abroad. There are approximately 33 JCI (Joint commission international) accredited hospitals in India. Medical visa on arrival scheme allows foreign patients to stay about a month (extendable upto 6 months) which decreases the difficulty of foreign travel and contributes substantially to the tourism growth.

Table 12: Long term complications and their management [1,4,65].

<table>
<thead>
<tr>
<th>Complication</th>
<th>Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychological disturbances</td>
<td>Counselling, Anxiolytics, antidepressants, psychotherapy</td>
</tr>
<tr>
<td>Thyroid disorders</td>
<td>6 monthly T3, T4, TSH</td>
</tr>
<tr>
<td>Lung damage</td>
<td>Pulmonary function tests</td>
</tr>
<tr>
<td>Infection</td>
<td>Hand wash</td>
</tr>
<tr>
<td>Infertility</td>
<td>Ova and sperm preservation, infertility clinics</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>Vitamin D and calcium supplements, exercise, weight bearing, DEXA scan</td>
</tr>
<tr>
<td>Skin rashes</td>
<td>Antivirals for herpetic infections, sunscreens, avoiding direct sunlight</td>
</tr>
<tr>
<td>Second malignancies</td>
<td>Annual pap smear, breast examinations and mammography, viral markers, colonoscopy, stool occult blood</td>
</tr>
<tr>
<td>Dental complications</td>
<td>Good oral hygiene, avoid dental procedures in first 6 months, routine dental examinations</td>
</tr>
<tr>
<td>Growth disturbances</td>
<td>Regular height and weight, if necessary growth hormone levels</td>
</tr>
<tr>
<td>Relapse of cancer</td>
<td>CBC, scheduled imaging as necessary</td>
</tr>
<tr>
<td>Hemorrhagic cysts</td>
<td>Watch for hematuria</td>
</tr>
</tbody>
</table>

Table 13: summarizing latest scientific reports with their inputs in ASCT activity in India [37-65].

<table>
<thead>
<tr>
<th>Reference</th>
<th>Analysis</th>
<th>Institution</th>
<th>Contribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kulkarni and George [60]</td>
<td>Access to hematopoietic stem-cell transplantation in India</td>
<td>Christian Medical College, Vellore, Tamil Nadu</td>
<td>Addresses multipronged approach that includes increasing the number and improving minimum standards for HSCT centers, reducing overall costs associated with HSCT, and helping patients with financial support for HSCT.</td>
</tr>
<tr>
<td>Das, et al. [61]</td>
<td>Establishing Hematopoietic Stem Cell Transplant Unit in Resource Limited Setting</td>
<td>Cancer Research Institute, Swami Rama Himalayan University, Dehradun</td>
<td>Criticism on criteria of qualified doctor and staff. Criticism on restriction on rare indications, not defining criteria and timing of establishing HSCT unit.</td>
</tr>
<tr>
<td>Jotwani [63]</td>
<td>National Guidelines for Stem Cell Research 2017</td>
<td>Indian Council of Medical Research and Department of Biotechnology</td>
<td>Any stem cell use in patients, other than that for hematopoietic stem cell reconstitution for approved indications, is investigational at present. Every use of stem cells in patients outside an approved clinical trial is unethical and shall be considered as malpractice.</td>
</tr>
<tr>
<td>Raut, et al. [52]</td>
<td>ASCT in HD</td>
<td>GCRI Ahmedabad</td>
<td>DFS 65% and OS 70%</td>
</tr>
<tr>
<td>Kumar, et al. [53]</td>
<td>ASCT for myeloma : long term results</td>
<td>AIIMS New Delhi</td>
<td>CR following ASCT associated with good long term outcome. PFS :32 months, OS : 85.5 months</td>
</tr>
<tr>
<td>Pandit, et al. [65]</td>
<td>Changes in bone mineral density and bone turnover markers in patients HSCT</td>
<td>Military Hospital, Shillong, Meghalaya</td>
<td>A significant bone loss is observed at 6 months in patients with post-HSCT predominantly at cortical bone. There is recovery at 12 months posttransplant except at Ward’s triangle.</td>
</tr>
<tr>
<td>Raut, et al. [54]</td>
<td>safety of eltrombopag in post HSCT thrombocytopenia</td>
<td>GCRI Ahmedabad</td>
<td>25-50 mg OD Ertrombopag for post-HSCT thrombocytopenia is well tolerated, appears efficacious and offers transfusion independence.</td>
</tr>
<tr>
<td>Shah C A, et al. [41]</td>
<td>data from western India</td>
<td>Apollo hospital, Gandhi Nagar</td>
<td>comparability with international standards</td>
</tr>
<tr>
<td>Shah C A, et al. [55]</td>
<td>ASCT in MM in nonuniversity hospital of developing country</td>
<td>Apollo hospital, Gandhi Nagar</td>
<td>ASCT feasible in nonuniversity hospital</td>
</tr>
<tr>
<td>Sharma, et al. [39]</td>
<td>cost of HSCT in India</td>
<td>BLK superspeciality hospital New Delhi</td>
<td>ASCT cost 12500 USD (10331-39367)</td>
</tr>
<tr>
<td>Kumar, et al. [52]</td>
<td>CR after ASCT in MM</td>
<td>AIIMS New Delhi</td>
<td>those who receive one line of induction therapy before transplant have superior outcome.</td>
</tr>
<tr>
<td>Kayaial, et al. [47]</td>
<td>ASCT using noncryopreserved peripheral blood stem cells</td>
<td>AIIMS New Delhi</td>
<td>Noncryopreserved PBSC is simple, effective and safe.</td>
</tr>
<tr>
<td>Mukhopadhyay [42]</td>
<td>data from Eastern India</td>
<td>NCRI Kolkata</td>
<td>ASCT cost 3-4 lakhs</td>
</tr>
<tr>
<td>Kumar L, et al. [49]</td>
<td>ASCT for HL and NHL</td>
<td>AIIMS New Delhi</td>
<td>pretransplant chemosensitive disease and CR after transplant had better survival</td>
</tr>
<tr>
<td>Pandya, et al. [62]</td>
<td>Ethics of stem cell transplant in India</td>
<td>Jaslok Hospital and Research Centre, Mumbai</td>
<td>Raised question on irradiation use of stem cells.</td>
</tr>
<tr>
<td>Chandey, et al. [37]</td>
<td>Stem Cell Transplantation In India.</td>
<td>CMC Vellore</td>
<td>First comprehensive Indian data on stem cell transplantation</td>
</tr>
</tbody>
</table>
patients taking treatment in India. Table 13 summarises contributing literature in ASCT from recent past in India.

**Conflict of Interest**

Author declared no conflicts of interest in any form.

**References**


57. Indian Stem Cell Transplant Registry (ISCTR) Indian Stem Cell Transplant.


