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EDITORIAL

Stem Cell Transplantation in Multiple Myeloma: Very Much Alive and Kicking

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Multiple myeloma is the second commonest hematological malignancy with rising incidence across the globe [1]. Myeloma afflicts individuals a decade younger in our country with a median age in the 4–5th decade as compared to subjects with Indian descents living in the US [2–4]. The younger population in our country also present with higher ISS stage and extramedullary disease. The treatment landscape of patients with myeloma has significantly improved in the last decade. The first significant advancement was the use of high dose chemotherapy followed by autologous stem cell transplantation in the 1990s. Since the beginning of 2000, many novel antimyeloma drugs with different mechanisms of actions were developed. In the last decade, there was further refinement and newer generation antimyeloma drugs and have come to use in the clinical practice quite quickly [5]. This has led to an improvement in median survival of myeloma patients from 3 to 4 years to more than 10 years in standard risk patients. The novel and novel–novel antimyeloma drugs are so effective that they are challenging the role of autologous stem cell transplantation in the treatment of multiple myeloma [3]. However, the fact is that myeloma remains an incurable illness for the majority of patients.

The stem cell transplantation program in India was initiated in 1980 at a handful of centers. In the last decade, the number of transplant centers in India have gone up considerably and so is the number of transplants. Figures available from ISCTR suggest myeloma transplants rising number from 154/year to 739/year in the last 10 years. From 1983 to 2016, of the total 12,340 transplants in India, 21% were for plasma cell dyscrasia and myeloma. Of the 4927 autologous transplants during this period, 52% were for plasma cell dyscrasia and myeloma [6]. Also, over the years, the post-transplant outcomes have improved with increasing standards of hygiene, availability of better antimicrobials, better post-transplant care and raising educational standards of the patients (better understanding of the disease biology). In this edition of the journal, Kulkarni et al. [7] described the outcomes of autologous transplantation from a center in South India. The authors have summarized the results from the top three institutes. Outcomes of transplantation in multiple myeloma from various other centers of India have been summarized in Table 1 [8].

There are few challenges for extending transplantation benefits which are specific to our country. The median time to transplantation still averages around ten months in our country from the time of diagnosis (Table 1); this could be attributed to the delayed decision making, poor education status and time taken for arranging finances [7, 9–13]. Lack of universal health care precludes many patients from the benefit of transplantation. The cost–benefit analysis of transplantation versus no transplantation has been studied previously [14, 15]. It showed marginal benefit in favor of transplant. However, the comparative arm was melphalan/prednisolone. It is well established that single myeloma transplant can be carried out without cryopreservation of stem cells thus cutting down on the cost of transplant. However, cryopreservation would be necessary if two or more transplants are required in the treatment of myeloma, a treatment option that is gradually decreasing with the

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Table 1 Outcomes of transplantation in multiple myeloma from various other centers of India

	Kumar et al. [19]	Malhotra et al. [9]	Kulkarni et al. [7]	Aggarwal et al. [11]	Gokarn et al. [13]	Naithani et al. [8]	Yanamandra et al. [20]
Institute	All India Institute of Medical Sciences, Delhi	Post Graduate Institute Medical Education Research, Chandigarh	Christian Medical College, Vellore	Rajiv Gandhi Cancer Institute, Delhi	Tata memorial hospital, Mumbai	Max Hospital, Saket	Army Hospital (Research and Referral), Delhi
N	225	94	245	141	85	50	172
Median time to transplant from diagnosis (months)	10	10.5	10.5	7	10.5	NR	NR
Median Age of Patients (y)	53	53	51	55	49	56	52
Pre-transplant response	≥ VGPR—44%	CR—42%, VGPR—39%, PR—14%	CR—19%, VGPR—37%, PR—37%	≥ VGPR—51.7%, PR—48.2%	CR—33%, VGPR—39%, PR—21%	CR—62%, VGPR—6%, PR—10%, Active—2%	NR
Post-transplant response	≥ VGPR—74%	NR	94.4%	83% (≥ VGPR)	89.5% (73% ≥ VGPR)	CR—44%, VGPR—6%, PR—8%, Relapse/progression—30%	NR
Predominant ISS Stage	ISS II	ISS III	ISS II	ISS I	ISS III	NR	ISS III
Commonest Subtype of plasma cell dyscrasia	IgG Kappa	IgG Kappa	NR	NR	IgG	NR	NR
Neutrophil Engraftment (Median, days)	NR	11	NR	10	NR	11	NR
Platelet Engraftment (Median, days)	NR	12	NR	11	NR	11	NR
TRM	7.2%	3.19%	2.86%	2.1%	NR	2%	3.4%
OS	63.2% (5 years)	76.7% (6.5 years)	61.6% (5 years)	72% (5 years)	91% (3 years)	86% (1.4 years)	72% (5 years)
PFS	38.5% (5 years)	55.8% (6.5 years) (biochemical)	37.2% (5 years)	36% (5 years)	58% (3 years)	NR	49%(5 years)

availability of novel drugs. Availability of HEPA filtered rooms for transplantation is a significant challenge in the govt sector, with few centers studying the transplantation in non-HEPA filtered rooms [16]. Though out-patient transplants are a routine in western countries, in Indian scenarios it is still a far-fetched dream considering the background hygiene, lack of good/prompt emergency services trained for handling out-patient transplants, most importantly education status of the caregivers/patient for understanding the nitty–gritty/care involved in these procedures. The current study by Kulkarni et al. also highlights the incidence of fungal infections to be around 4.5% when antifungal prophylaxis was not used. Invasive fungal infection is the primary cause of mortality in management of hematological diseases in our country as was responsible for 50% mortality in this series as well [17]. This is an

important aspect when considering a transplant in developing countries where the environment plays a significant role in precipitating infections and rakes debate on routine antifungal prophylaxis.

Role of allogeneic transplantation in Myeloma is debatable. The number of allogeneic transplants for plasma cell dyscrasias in India account for 1% of the total allogeneic transplants as per the ISCTR data [6]. It is reserved for the younger, high-risk patients, and those who have relapsed after the autologous transplantation. In a recent review in the journal, Jaiswal et al. [18] have revisited the various challenges and the benefits of the procedure, particularly in the Indian setting.

With the advent of the newer drugs in the management of the myeloma and their increasing availability in the country, there is always a fear of abandoning the transplants in myeloma. However, considering the increased costs of monoclonal antibodies and the newer drugs, and the falling costs of the myeloma transplants and a growing number of transplants, the role of autologous stem cell transplant is here to stay, alive and kicking.

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Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

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