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– ORIGINAL PAPER –

Retrospective Analysis of Patients with Multiple Myeloma Post Autologous Stem Cell Transplant

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Abstract

Introduction: *Multiple myeloma is a plasma cell disorder characterised by hypercalcaemia, renal dysfunction, and anaemia with bony lytic lesions. While multiple myeloma remains incurable, advancements in treatment have significantly improved patient outcomes. The choice of treatment depends on factors such as disease stage, patient age, overall health, and specific genetic abnormalities if present. Induction therapy typically includes proteasome inhibitors and dexamethasone with immunomodulators. Following induction, an autologous stem cell transplant is recommended as a consolidative therapy for multiple myeloma. In our study, we retrospectively analysed 40 patients with multiple myeloma who underwent autologous stem cell transplants between January 2020 and December 2024.*

Aim*: To assess disease characteristics, transplant-related complications, and outcomes in patients undergoing autologous stem cell transplant for multiple myeloma.*

Results: *A total of 40 patients were evaluated. 32 (80%) were male, and 8 (20%) were female. Of these, 20 were under 50 years old, and 20 were over 50 years old. The most common co-morbidity was hypertension (HTN) in 6 (15%). Twenty-one (52.5%) had IgG Kappa disease. Twenty-four (60%) patients were in ISS I at the time of transplant. The most frequently used chemotherapy was VRD (Bortezomib, Lenalidomide, and Dexamethasone) in 33 (82.5%) cases. The disease assessment after chemotherapy showed that 18 (45%) patients achieved VGPR; 13 (32.5%) were in CR; and 9 (22.5%) were in PR before undergoing stem cell transplant. All patients received Inj Melphalan 200 mg/m2 or 140 mg/m2 as a conditioning regimen. The median stem cell dose was 7.54 x 10^6 cells/kg (interquartile range 2.59–23.9 million cells/kg). Transplant-related complications included febrile neutropenia in 39 (96%), mucositis in 40 (100%), vomiting in 36 (90%), pneumonia in 5 (12.5%), and perianal complications in 12 (30%) patients. The mean hospital stay from stem cell rescue to discharge was 12 days. No mortality was observed during the hospital stay or until 100 days after the stem cell transplant. At a median follow-up of 21 months, biochemical relapse was documented in 5 (12.5%) patients, while clinical relapse occurred in 4 (10%). Overall survival at 12 months was 97.5%.*

Conclusion: *Day 30 and Day 100 mortality was 0%, with a 1-year survival rate of 97.5% (at a median follow-up of 21 months). The 1-year cumulative probability of event-free survival was 87.5%.*

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Introduction

Multiple myeloma is a plasma cell disorder characterised by hypercalcaemia, renal dysfunction, and anaemia with bony lytic lesions. Although multiple myeloma remains incurable, advances in treatment have significantly improved patient outcomes. The choice of treatment depends on factors such as disease stage, patient age, overall health, and specific genetic abnormalities present. Secretory myelomas are classified into IgG, IgM, IgA, IgD, IgE, lambda, or kappa light chain disease. The most common types of myeloma are IgG, while IgA myelomas are less common; however, bony involvement tends to be more frequent in the IgA type. [1][2][3]

Induction therapy typically involves proteasome inhibitors and dexamethasone combined with immunomodulators. The treatment regimen for multiple myeloma using bortezomib, lenalidomide, or cyclophosphamide, along with dexamethasone, is considered the first-line therapy. In high-risk mutations, aggressive management with second-line therapy as frontline treatment is advised.[4] Initial complications include peripheral neuropathy, constipation or diarrhoea, darkening of the skin, or cytopenia secondary to lenalidomide, as well as hyperglycemia.[5] After induction and response evaluation, an autologous stem cell transplant is recommended as a consolidative treatment. The response assessment categorises patients into complete response, very good partial response, and partial response for those undergoing autologous stem cell transplant in multiple myeloma. A patient should achieve at least a partial response before proceeding with the autologous stem cell transplant, as lower responses are associated with poor outcomes.[6]

Complications of autologous stem cell transplant include febrile neutropenia, mucositis, intractable vomiting, multiple blood product transfusions, pneumonia, and, in some cases, respiratory failure. Pneumonia is usually caused by gram-negative sepsis, leading to respiratory failure.[7] Due to severe mucositis and inability to eat orally, these patients often require parenteral nutrition, which can cause electrolyte imbalances.[8] Occasionally, prolonged neutropenia resulting from delayed count recovery and grade III-IV mucositis necessitates long-term parenteral nutrition, which may lead to lethal refeeding syndrome upon reintroduction of feeding by any means.[8]

Material and methods

In our study, we retrospectively analysed 40 patients with multiple myeloma who underwent autologous stem cell transplants between January 2020 and December 2024 at the Department of Clinical Hematology, Mahatma Gandhi Medical College, Jaipur, India. All diagnosed cases of multiple myeloma treated with a bone marrow transplant at MGH were included in the study. Baseline data, including clinical characteristics at initial presentation, as well as additional factors such as details of therapy, complications, and outcomes, were documented. Data regarding disease characteristics, transplant-related complications, and outcomes in patients undergoing autologous stem cell transplants for multiple myeloma were recorded. Response to treatment in multiple myeloma was defined according to the International Myeloma Working Group. Complete remission was defined as negative immunofixation on blood and urine, with no plasmacytoma and fewer than 5% plasma cells; VGPR was defined as > 90% reduction in the M band plus

urine protein level <100 mg/24 hour or serum or urine M protein detectable by immunofixation while negative on electrophoresis. Partial response was defined as >50% reduction in the serum M protein or >50% decrease in the difference between involved and uninvolved light chains.[9] Ethical committee approval was obtained from the institutional committee (MGMC&H/IEC/JPR /2025/4513)

Statistical analysis - The qualitative data were presented as proportions and percentages, while the quantitative data were expressed as means and standard deviations [or median (IQR)]. Appropriate statistical tests will be employed to identify significant associations, with a p-value <0.05 regarded as statistically significant.

Result

A total of 40 patients were evaluated. 32 (80%) patients were male and 8 (20%) were female. Out of 40 patients, 20 were <50 years old, while 20 were >50 years old. The most common co-morbidity was HTN (Hypertension) in 6 (15%), DM (Diabetes Mellitus) in 4 (10%), hypothyroidism, and CAD (Coronary Artery Disease) in each 1 (2.5%) patient. On characterisation, 21 (52.5%) patients had IgG Kappa disease; 7 (17.5%) IgG Lambda; 7 (17.5%) Kappa light chain disease; 3 (7.5%) IgA Kappa disease, while 2 (5%) had lambda light chain disease. On staging, 24 (60%) patients were in ISS I, 7 (17.5%) in ISS II, and 9 (22.5%) in ISS III at the time of transplant. The most common chemotherapy received was VRD (Bortezomib, Lenalidomide, and Dexamethasone) in 33 (82.5%); Daratumumab + VRD in 3 (7.5%); VCD (Bortezomib, Cyclophosphamide, and Dexamethasone), VCD followed by VRD, Daratumumab + VCD, VRD + Daratumumab + Carfilzomib, each in 1 (2.5%) patient. In response assessment, 21 (53.5%) patients were in VGPR; 13 (32.5%) in CR; 6 (15%) in PR. In the younger age group (≤50 years), 19 patients received VRD or VCD induction chemotherapy, while one patient received Daratumumab in frontline treatment. Of the 20 patients in the >50 age group, 18 received either VCD or VRD chemotherapy, and two received Daratumumab in frontline management. Four patients achieved at least a partial response (PR) after induction chemotherapy in the age group below 50. In patients over 50, only two achieved at least PR. All patients except 2 received Inj Melphalan 200 mg/m2 as a conditioning regimen; two patients received Inj Melphalan 140 mg/m2. The median stem cell dose received was 7.54 x 10^6 cells/kg (IQR 2.59–23.9 million cells/kg). Neutrophil engraftment (median) occurred on Day +10 (8-14 days); platelet engraftment (median) occurred on Day +12 (9-18 days). Transplant complications included febrile neutropenia in nearly all individuals, 39 (96%); mucositis in 40 (100%); vomiting in 36 (90%); pneumonia in 5 (12.5%); and perianal complications in 12 (30%). Parenteral nutrition was given to 28 (70%) patients. The mean duration of parenteralnutrition was 4 days. The mean hospital stay from stem cell rescue to discharge was 12 days. No mortality was observed during the hospital stay or until 100 days after the stem cell transplant. At a median follow-up of 21 months, biochemical relapse was documented in 5 (12.5%) patients, while clinical relapse was observed in 4 (10%). Overall survival at 12 months was 97.5%. Median OS was not achieved.

Discussion

Multiple myeloma is a haematological malignancy that, although incurable, requires lifelong management. Advances in treatment have significantly improved overall survival rates. The disease's epidemiology suggests a higher prevalence among the elderly; however, in our study, 20 patients were under 50 years of age. This shift may be due to increased awareness and easier access to testing. Obesity was identified as a factor associated with multiple myeloma.[10] Among 40 patients in our study, 15 (37.5%) were obese according to the Asian WHO criteria. Multiple myeloma in younger patients is noted to be resistant in some studies and linked to a higher likelihood of extramedullary disease and high-risk genetics.[11] In our study, of 20 patients in the ≤50 age group, 19 received either VCD or VRD chemotherapy, and only one patient received Daratumumab in frontline management. Four patients achieved at least a partial response (PR) after induction chemotherapy in the age group below 50. However, in comparison with patients over 50, only 2 of the remaining 20 patients received Daratumumab, with two patients achieving at least PR. Overall, there was no difference between younger and older patients regarding the magnitude of response before undergoing stem cell transplant in our study; however, other studies have demonstrated a high rate of response in younger individuals.[12]

Prior chemotherapy affects stem cell mobilisation. Patients with a history of significant cytotoxic drug intake and multiple previous lines of treatment are more likely to have low stem cell yields. Studies showed that each additional cycle of VRD results in a decrease in stem cell yield by 0.5846 × 10^6/kg.[13] Patients undergoing local

site radiotherapy involving bone marrow also tend to have lower stem cell yields. In our study, among patients who received VRD as induction therapy, only one had a stem cell yield of < 3 × 10^6/kg, and two patients underwent a second harvest due to low stem cell yield; moreover, two patients with a history of radiotherapy to the local site had yields >10 × 10^6/kg, indicating that the cause of failed stem cell mobilisation could be multifactorial.[14]

Studies show that lower doses of stem cells are linked to delayed engraftment. [15] Few studies mention the role of ongoing antibiotics in engraftment. In our research, neutrophil engraftment (median) occurred on Day+10 (range 8-14 days), while platelet engraftment (median) occurred on Day+12 (range 9-18 days), which is comparable to other studies. [16] Some studies also indicate a correlation between the time since melphalan infusion and engraftment, revealing that stem cell rescue administered within 24 hours of melphalan injection affects platelet and neutrophil engraftment; however, another study found no significant difference. In our research, stem cell rescue was given after 24 hours of the melphalan injection according to our institute's policy, and engraftment times were consistent with other studies. [16][17] In our study, 70% of patients received parenteral nutrition with a mean duration of 4 days. Parenteral nutrition delays platelet engraftment through mechanisms that are not fully understood.[18] However, in our study, platelet engraftment was achieved on a median day +12, which aligns with other studies.[16]

Post conditioning protocol in the setting of stem cell transplant, febrile neutropenia is often accompanied by an array of bacterial, fungal, and parasitic infections. Most common complication was oral mucositis in 40(100%), febrile neutropenia 39(96%); vomiting in 36(90%); Pneumonia in 5(12.5%); Perianal complications in 12(30%) in our study. Other studies also had the same spectrum of complications in multiple myeloma patients. [19] Our patient received levofloxacin prophylaxis on discharge, and no patient required admission within +30 days or +100 days from the date of the transplant, with no mortality within 100 days. In contrast, the empirical levofloxacin prophylaxis, however, showed no benefit in another study. [20]

In our study, overall survival at 12 months was 97.5% (Image 1). At a median follow-up of 21 months, biochemical relapse was documented in 5 (12.5%) patients, while clinical relapse was observed in 4 (10%). The 1-year cumulative probability of event-free survival was 87.5%. Our findings align with other studies, showing an overall survival of 93.5%.[21] In our research, cytogenetic abnormalities were not considered, as many patients did not have them at baseline, which is a limitation of the study.

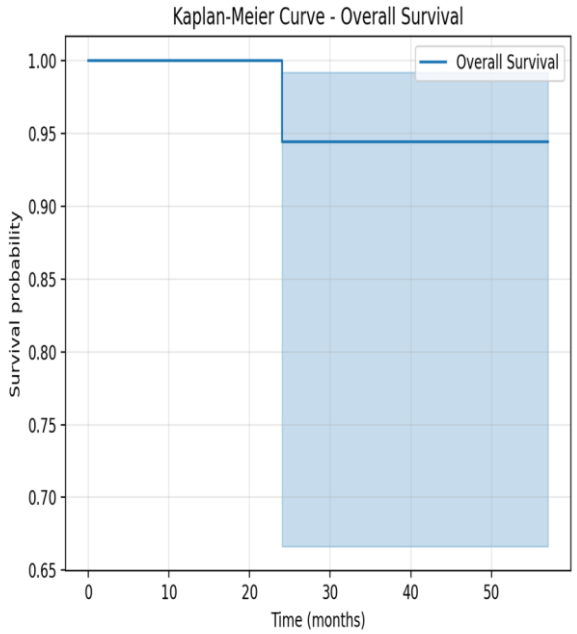

***Image 1**: Overall survival of patients with multiple myeloma at 1 year*

Total patients	40
Male	32(80%)
Female	8(20%)
Age	
Age≤50 years	20(50%)
Age> 51 years	20(50%)
Comorbidities	
HTN	6 (15%)
DM	4 (10%)
Hypothyroidism	1 (2.5%)
CAD	1 (2.5%)
Type	
IgG kappa	21(52.5%)
IgG lambda	07(17.5%)
IgA kappa	07(17.5%)
Kappa light chain disease	03(7.5%)
Lambda light chain disease	02(5%)
Stage	
ISS I	24(60%)
ISS II	07(22.5%)
ISS III	09(22.5%)
Treatment received	
VRD	33(82.5%)
Daratumumab+ VRD	03(7.5%)
VCD	01(2.5%)
VCD+VRD	01(2.5%)
Daratumumab+ VCD	01(2.5%)
VRD+Daratumumab+Carfilzomib	01(2.5%)

Table 1: *Baseline characteristics of enrolled patients with multiple myeloma.*

Response status at transplant	
PR	06(15%)
VGPR	21(52.5%)
CR	13(32.5%)
Need of 2nd harvest	
YES	2(05%)
Melphalan conditioning dose	
200mg/m2	38(95%)
140 mg/m2	02(05%)

Table 2*: Response status of patients before stem cell transplant and conditioning regimen used*

Conclusion

Day 30 and Day 100 mortality was 0%, with a 1-year survival rate of 97.5% (at a median follow-up of 21 months). The 1-year cumulative probability of event-free survival was 87.5%.

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Ethical considerations: The research was conducted in accordance with the Declaration of Helsinki, and patient consent was obtained.

Conflict of interest
We certify that we do not have any financial or personal relationships that might bias the content of this work.

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