

Clinical Profile of Multiple Myeloma in South India

Abstract

Background: The incidence of multiple myeloma (MM) is known to be variable according to ethnicity and is increasing rapidly in Asian countries. Because of huge disparities in economy, lack of adequate health-care infrastructure and the lack of access to novel drugs in our country, treatment of multiple myeloma is still a challenge to medical field in India. **Methods:** This was a descriptive longitudinal study conducted in the medicine and oncology units of a tertiary care hospital in south India. During the one year period of data collection, 37 cases of multiple myeloma were diagnosed, of which 5 cases were excluded. The diagnosis of MM was made based on the International Myeloma Working Group: Criteria for the classification of monoclonal gammopathies, multiple myeloma and related disorders. The clinical and laboratory characteristics, and treatment were studied. **Results:** The male to female ratio was 1.3:1. The commonest symptoms noticed were fatigue 32 (100%) and bone pain 31 (96.9%). 6 (18.8%) patients had hypercalcemia and 7 (21.9%) patients had elevated serum creatinine levels. 29 (91%) of 32 had lytic lesions in the skull and 27 (84%) had lytic lesions in the spine. One patient expired during the course of the treatment. 20 (64%) of 32 patients had partial response to treatment, 7 (23%) had complete response and 4 (13%) of them had stable disease not responding to treatment. **Conclusions:** To conclude, the patients with multiple myeloma in the present study had a male preponderance. Most common symptoms noticed were fatigue and bone pain and majority had spine tenderness on examination. The presentation of MM is non-specific and patient can come with varied presentations at onset. The quality of life and survival in MM patients can be improved significantly if there is access to newer therapies.

Keywords: Clinical profile, multiple myeloma, South India

Introduction

The incidence of multiple myeloma (MM) is increasing rapidly in Asian countries.^[1,2] MM will eventually become a tremendous medical burden in this region, challenging the health-care systems of Asian countries.^[1,2] Because of huge disparities in economy, lack of adequate health-care infrastructure and the lack of access to novel drugs in our country, treatment of MM is still a challenge to medical field in India. The incidence of myeloma is highest in African-American and Pacific islanders, intermediate in Europeans and North Americans and lowest in developing countries including Asia.^[3] In India, the estimated incidence according to Globocan 2012 is 6955 new cases, mortality of 6027 and 5 years' prevalence estimate of 11886.^[4] In the annual report (2013–2014) published by regional cancer center, Thiruvananthapuram, Kerala, there were 258 (2%) cases of MM.^[5]

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

MM is characterized by malignant proliferation of plasma cells derived from a single clone. The introduction of novel agents such as thalidomide, lenalidomide, and bortezomib had a profound impact on treatment and survival. There are various chemotherapeutic options available for MM. Autologous stem cell transplant should be considered in selected patients after the induction treatment.^[6] There are very few studies related to MM from India. This study thus aims to study the clinical profile and treatment of MM patients in our part of the country.

Subjects and Methods

This was a descriptive longitudinal study conducted in the medicine and oncology units of a tertiary care hospital (M. E. S Medical College, Perinthalmanna) in South India after obtaining approval from the institutional Ethical Committee (No. IEC/MES/74/2014). During the 1-year period of data collection (January 01–December 31, 2015), 37 cases

How to cite this article: Fousad C, Gangadharan KV, Abdulla MC, Naryan R, Mohammed Ali MJ. Clinical profile of multiple myeloma in South India. Indian J Med Paediatr Oncol 2018;39:62-6.

Chemban Fousad, KV Gangadharan¹, Mansoor C Abdulla, Ram Naryan, M Jesha Mohammed Ali²

Departments of General Medicine, ¹Oncology and ²Community Medicine, M.E.S. Medical College, Perinthalmanna, Kerala, India

Address for correspondence:

Dr. Mansoor C Abdulla,
Department of General
Medicine, M.E.S. Medical
College, Perinthalmanna,
Kerala, India.
E-mail: drcamans@gmail.com

Access this article online

Website: www.ijmpo.org

DOI: 10.4103/ijmpo.ijmpo_57_17

Quick Response Code:



of MM were diagnosed, of which 5 cases were excluded as they were not willing to continue treatment from our hospital and lost follow-up. The remaining 32 cases were enrolled for the study. The diagnosis of MM was made based on the International Myeloma Working Group: criteria for the classification of monoclonal gammopathies, MM, and related disorders.^[7]

An informed written consent was obtained from those enrolled for the study. A detailed history included; patient particulars such as name, age, contact details, sex, occupation, marital status, religion, education, family income, and symptoms of MM. The socioeconomic status was classified according to BG Prasad's socioeconomic classification. A detailed clinical examination was also done.

A complete workup including blood counts, erythrocyte sedimentation rate, liver function test, renal function test, serum calcium, peripheral smear, bone marrow study, serum protein electrophoresis, urine routine, presence of urine Bence-Jones proteinuria, skeletal survey (skull and spine X-rays) were performed. Serum protein electrophoresis was done by agarose gel electrophoresis. Bone marrow study and peripheral smear were reported by experts from pathology. The effect and outcome of treatment were analyzed at four and 6 months from the commencement of treatment. The treatment given was the standard treatment regime. The follow-up was assessed with clinical profile, serum protein electrophoresis, and bone marrow study.

Data analysis

For the statistical analysis, the statistical software SPSS version 16.0 for Windows (SPSS Inc., Chicago, IL, USA) was used. A comparison of mean bone marrow plasma cell percentage before and after the treatment was done using paired *t*-test with *t* value of 4.138 (degree of freedom = 30) and *P* = 0.0001.

Results

Thirty-seven cases of MM were diagnosed during the study period, but 5 cases were excluded as they were not willing to continue treatment from our hospital and lost follow-up. The remaining 32 cases were enrolled for the study.

Sociodemographic profile

Of 32 patients, 14 (44%) were female and 18 (56%) were male. The male to female ratio was 1.3:1. The age of patients ranged from 39 to 83 years with a mean age of 64 ± 10.77 years. Seventh decade was found to be the most common age group in our study population. All the females were homemaker. Among males, 58.8% were manual laborers, 35.3% were unemployed, and 5.9% were unskilled workers. Majority 25 (78%) belonged to Class IV according to BG Prasad's socioeconomic classification.^[8] Thirty-one (97%) patients consumed a mixed diet and only 1 (3%) was pure vegetarian. Sixteen (50%) patients were smokers, 6 (18.8%) chewed tobacco, and 7 (21.9%)

consumed alcohol. Eight (25%) patients had a history of diabetes mellitus and systemic hypertension. There was history of fracture bone/vertebrae in the past among 20 (63%) of the participants. History of recurrent infections was reported by 13 (41%).

Clinical features

The most common symptoms noticed were fatigue 32 (100%) and bone pain 31 (96.9%). Of the 32 patients, 29 (90.6%) had pallor. Clinical characteristics are summarized in Table 1.

Lab investigations

Sixteen patients (50%) had anemia according to the criteria satisfying myeloma-related tissue or organ impairment (Hb <10 g/dL). Majority 29 (90.6%) of patients had normal white blood cell count, 2 (6.3%) of them had leukocytosis and 1 (3.1%) had leukopenia. Five (15.6%) cases had thrombocytopenia. Laboratory characteristics are summarized in Table 2. All patients had bone marrow plasmacytosis more than 10% on marrow examination. The percentage of plasma cells >70% was seen in 2 (6.3%) cases and between 50% and 70% in 3 (9.4%) and between 10% and 30% in 19 (59.4%) cases of study population. The mean bone marrow plasma cell percentage before therapy was found to be $31.26\% \pm 19.97\%$.

Table 1: Clinical characteristics of patients (n=32)

Clinical feature	n (%)
Pallor	29 (90.6)
Spine tenderness	29 (90.6)
Oedema	17 (53.1)
Localized bony swelling	4 (12.5)
Fatigue	32 (100)
Bone pain	31 (96.9)
Low back ache	31 (96.9)
Weight loss	27 (84.4)
Fever	18 (56.3)
Peripheral neuropathy	8 (25)
Nausea and vomiting	5 (15.6)
Bony swelling	4 (12.5)

Table 2: Laboratory findings of the patients (n=32)

Investigations	n (%)
Anemia	16 (50)
Thrombocytopenia	5 (15.6)
Elevated ESR	32 (100)
Hypercalcemia	6 (18.8)
Elevated serum creatinine levels	7 (21.9)
Low serum albumin	20 (62.5)
Urine Bence-Jones proteinuria	3 (9.4)
Serum protein electrophoresis showing M band	30 (94)
X-ray skull - lytic lesions	29 (90.6)
X-ray spine - lytic lesions	27 (84.4)
ESR – Erythrocyte sedimentation rate	

Treatment and outcome

Thirteen (40.6%) of 32 received cyclophosphamide, dexamethasone, and thalidomide regimen. Three (9.4%) patients received bortezomib, dexamethasone, and thalidomide regimen. Two (6.3%) of them received bortezomib, cyclophosphamide, and thalidomide regimen. Five (15.6%) cases received dexamethasone and thalidomide regimen. Of 32 patients, one patient expired during the treatment. The follow-up assessment showed that 20 (64%) of 32 patients had partial response to treatment and 7 (23%) had complete response. Four (13%) of them had stable disease not responding to treatment. All the patients who achieved either partial or complete response following treatment had a significant reduction in bone pain. It was noticed that one patient during the treatment complained of significant loss of appetite and weight with bleeding per rectum and melena. Further evaluation revealed moderately differentiating adenocarcinoma of stomach. Among the 13 (40.6%) patients who received cyclophosphamide, dexamethasone, and thalidomide regime, 4 (13%) had stable disease not responding to treatment. All the patients who received bortezomib therapy showed either partial or complete response and none of them had stable or progressive disease.

The mean bone marrow plasma cell percentage after therapy was 13.29% compared to 31.26% before therapy. The comparison of means showed a significant difference between the mean plasma cell percentage before and after the treatment ($t = 4.138$ [degree of freedom = 30] and $P = 0.0001$).

Discussion

A high male:female ratio in our study was similar to the United Kingdom cancer research statistics in 2013 (57% males and 43% in women), giving a male:female ratio of 1.3:1.^[9] Seventh decade was found to be the most common age group in our study population and the mean age was 64 ± 10.77 years. Sixth decade was the most common age group at presentation in Asian myeloma network study^[10] and an Indian study by Kaur *et al.*^[11] The most common symptoms were fatigue 32 (100%) and bone pain 31 (96.9%). Kyle *et al.*,^[12] from mayo clinic in Rochester, reported bone pain as the predominant symptom (68%). Majority of our study population (29, 90.6%) had spine tenderness on examination. Most common clinical presentation (56%) was bone related such as bony swelling, bone pain, low backache, and pathological fractures in an Indian study.^[13]

Sixteen (50%) patients had anemia according to the criteria satisfying myeloma-related tissue or organ impairment (Hb <10 g/dL) as in previous studies. The reason for anemia in MM can be either as a result of renal impairment or can be due to bone marrow failure because of marrow infiltration by myeloma cells. Thrombocytopenia,

which might be due to marrow infiltration by myeloma cells, was observed in 5 (15.6%) cases as in previous studies.^[11]

Hypercalcemia, even though considered as one among the important diagnostic criteria (CRAB symptoms), was seen only in six (18.8%) patients. Kyle *et al.*^[12] also reported hypercalcemia only among 13% of the 1027 patients.^[12] Diagnosis of MM was made in those with normal calcium 21 (66%) and below normal levels 5 (16%). Low calcium levels might be due to renal impairment. However, 2 (6%) patients had low calcium levels without renal impairment. Hypocalcemia in MM secondary to Vitamin D deficiency was reported previously.^[14] Factors including vitamin D deficiency may be contributing to hypocalcemia other than renal failure in myeloma patients.

Renal impairment was seen only in 7 (21%) patients. Studies by Kyle *et al.*^[12] and Kaur *et al.*^[11] showed a significant renal impairment (55% and 86.4%, respectively). The underlying cause for renal failure in MM can be hypercalcemia or myeloma kidney itself. Low serum albumin level was found in majority of the patients 20 (62.5%). Combination of albumin and serum β_2 microglobulin forms the basis for a three stage international staging system that predicts survival.^[3] Serum albumin level was found to be a significant prognostic factor for assessing disease severity in symptomatic MM in a previous study.^[15]

Thirty (94%) patients had a thick M-band in serum protein electrophoresis and the most common site was the gamma globulin region. In the study by Kyle *et al.*,^[12] 82% had M-band.

Thirteen (40.6%) cases received cyclophosphamide, dexamethasone, and thalidomide regimen. Three (9.4%) of them received bortezomib, dexamethasone, and thalidomide regimen. Although bortezomib has showed good results in various studies,^[16,17] its use is limited in our center because of the financial burden and cost factor. The socioeconomic status of the patients being treated from our center, as already mentioned, majority comes under Class IV according to BG Prasad's socioeconomic classification, and hence, cost affordability is one of the important issues with bortezomib even though now being a good choice in frontline therapy of MM. Bortezomib can be part of any treatment regimen and lack of renal excretion helps in its use in patients presenting with renal failure. Use of subcutaneous administration and once-weekly schedule has decreased the neurological toxicity and allows for its extended use. Various studies also suggests its better efficacy and outcome and can be presently used as a first-line agent.^[18] Some studies also shows significant improvement in survival and better efficacy when used for induction and maintenance treatment as well as before and after autologous stem cell transplantation.^[19] After its approval by the US and European regulatory authorities for

the treatment of MM, there have been a large number of studies confirming better results with the drug.

Due to limitations in our study because of financial constraints of the study group, we were unable to do serum-free light chain assay as already mentioned previously which forms part of uniform response criteria for reassessment after treatment. Hence, it was not possible to strictly adhere with the uniform response criteria suggested by international myeloma working group. However, we reassessed the study group after treatment based on the disappearance of M-band by serum protein electrophoresis and reduction of bone marrow plasma cell percentage. The follow-up assessment showed that majority (64%) showed partial response to treatment and 7 (23%) showed complete response. Four (13%) of them had stable disease not responding to treatment. The mean bone marrow plasma cell percentage after therapy was 13.29% compared to 31.26% before therapy. A similar study showed that 10 (56%) patients had complete response and 8 (44%) had partial response.^[13] The mean bone marrow plasma cell percentage at the end of therapy was 2% compared to 56% before therapy in their study.^[13]

The reassessment of clinical features showed that all the patients who achieved either partial or complete response following treatment had a significant reduction in bone pain. One patient during the treatment had significant loss of appetite and weight with bleeding per rectum and melena. Further evaluation revealed moderately differentiating adenocarcinoma of stomach. A similar rare presentation of coexistent MM with gastric carcinoma was reported in a 77-year-old male patient.^[20]

Among the 13 (40.6%) cases who received cyclophosphamide, dexamethasone, and thalidomide regimen, 4 (13%) had stable disease not responding to treatment. All the 6 (19%) patients treated with bortezomib showed either partial or complete response showing the efficacy of bortezomib in our study population. The response achieved with bortezomib was much better than with cyclophosphamide, dexamethasone, and thalidomide regimen in our study group, as suggested by 4 (13%) of the patients having a stable or progressive disease with cyclophosphamide-based regimen and none had the same with bortezomib.

Conclusions

To conclude, the patients with MM in the present study had a male preponderance with a male to female ratio of 1.3:1. Seventh decade was found to be the most common age group at presentation. Most common symptoms noticed were fatigue and bone pain and majority had spine tenderness on examination. Hypercalcemia, even though considered as one among the important diagnostic criteria was seen in

few patients. The presentation of MM is nonspecific and patient can come with varied presentations at onset. The quality of life and survival in MM patients can be improved significantly if there is access to newer therapies.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Lee JH, Lee DS, Lee JJ, Chang YH, Jin JY, Jo DY, *et al.* Multiple myeloma in Korea: Past, present, and future perspectives. Experience of the Korean Multiple Myeloma Working Party. *Int J Hematol* 2010;92:52-7.
2. Huang SY, Yao M, Tang JL, Lee WC, Tsay W, Cheng AL, *et al.* Epidemiology of multiple myeloma in Taiwan: Increasing incidence for the past 25 years and higher prevalence of extramedullary myeloma in patients younger than 55 years. *Cancer* 2007;110:896-905.
3. Munshi NC, Longo DL, Anderson KC. Plasma cell disorders. In: Kasper DL, Fauci AS, Longo DL, Braunwald E, Hauser SL, Longo DL, *et al.*, editors. *Harrison's Principles of Internal Medicine*. 19th ed. New York: McGraw-Hill; 2015. p. 710-7.
4. Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, *et al.* Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11. Lyon, France: International Agency for Research on Cancer; 2013. Available from: http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx. [Last accessed on 2017 Jun 20].
5. Regional Cancer Centre, Annual Report 2013-2014. Available from: http://www.rcctvm.org/RCC_AR_2014-15.pdf. [Last accessed on 2017 Jun 27].
6. Moreau P, Avet-Loiseau H, Harousseau JL, Attal M. Current trends in autologous stem-cell transplantation for myeloma in the era of novel therapies. *J Clin Oncol* 2011;29:1898-906.
7. International Myeloma Working Group. Criteria for the classification of monoclonal gammopathies, multiple myeloma and related disorders: A report of the International Myeloma Working Group. *Br J Haematol* 2003;121:749-57.
8. Dudala SR, Reddy KA, Prabhu GR. Prasad's socio-economic status classification – An update for 2014. *Int J Res Health Sci* 2014;2:875-8.
9. Cancer Statistics, Cancer Research UK; 2013. Available from: <http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/myeloma>. [Last accessed on 2014].
10. Kim K, Lee JH, Kim JS, Min CK, Yoon SS, Shimizu K, *et al.* Clinical profiles of multiple myeloma in Asia-An Asian Myeloma Network study. *Am J Hematol* 2014;89:751-6.
11. Kaur P, Shah BS, Baja P. Multiple myeloma: A clinical and pathological profile. *Gulf J Oncolog* 2014;1:14-20.
12. Kyle RA, Gertz MA, Witzig TE, Lust JA, Lacy MQ, Dispenzieri A, *et al.* Review of 1027 patients with newly diagnosed multiple myeloma. *Mayo Clin Proc* 2003;78:21-33.
13. Sridhar S, Dutta TK, Basu D. Clinical profile of multiple myeloma and effect of thalidomide based treatment on its outcome. *J Indian Med Assoc* 2011;109:880-2, 887-8.
14. Ramasamy I. Hypocalcemia in multiple myeloma secondary to unrecognised Vitamin D deficiency: A case report. *Bone* 2011;48:S27-8.

15. Kim JE, Yoo C, Lee DH, Kim SW, Lee JS, Suh C. Serum albumin level is a significant prognostic factor reflecting disease severity in symptomatic multiple myeloma. *Ann Hematol* 2010;89:391-7.
16. Jagannath S, Durie BG, Wolf JL, Camacho ES, Irwin D, Lutzky J, *et al.* Extended follow-up of a phase 2 trial of bortezomib alone and in combination with dexamethasone for the frontline treatment of multiple myeloma. *Br J Haematol* 2009;146:619-26.
17. Painuly U, Kumar S. Efficacy of bortezomib as first-line treatment for patients with multiple myeloma. *Clin Med Insights Oncol* 2013;7:53-73.
18. Palumbo A, Bringhen S, Larocca A, Rossi D, Di Raimondo F, Magarotto V, *et al.* Bortezomib-melphalan-prednisone-thalidomide followed by maintenance with bortezomib-thalidomide compared with bortezomib-melphalan-prednisone for initial treatment of multiple myeloma: Updated follow-up and improved survival. *J Clin Oncol* 2014;32:634-40.
19. Neben K, Lokhorst HM, Jauch A, Bertsch U, Hielscher T, van der Holt B, *et al.* Administration of bortezomib before and after autologous stem cell transplantation improves outcome in multiple myeloma patients with deletion 17p. *Blood* 2012;119:940-8.
20. Demir C, Atmaca M, Tasdemir E and Efe S. Association of multiple myeloma and gastric adenocarcinoma. *J Clin Exp Invest* 2011;2:110-3.