

## Clinical profile of multiple myeloma in a tertiary medical college northern Kerala, India

Ramani P.N<sup>1\*</sup>, Sreeraj V<sup>2</sup>, Kanniyann Binub<sup>3</sup>

<sup>1-3</sup>Assistant Professor, <sup>1</sup>Dept. of General Medicine, <sup>3</sup>Dept. of Community Medicine, <sup>1</sup>Dr. Somervell Memorial CSI Medical College, Kerala, <sup>2</sup>Kerala Health Service, Kerala, <sup>3</sup>MES Medical College, Perinthalmanna, Kerala, India

**\*Corresponding Author: Ramani P.N**

Email: kanniyannbinub@gmail.com

### Abstract

**Introduction:** Multiple myeloma is a clonal plasma cell disorder which varies its clinical course ranging from relatively indolent form to frankly aggressive neoplasia.

**Objectives:** To study the clinical profile of Multiple myeloma.

**Materials and Methods:** Descriptive study was conducted at a tertiary medical College in Kerala. 70 patients of Multiple myeloma was found with help of laboratory work up including urine Bence Jones with heat coagulation method. Serum albumin, calcium, uric acid was also done using standard biochemical kits. X-ray of Thoracic, Lumbar spine, Humerus, Hip region was evaluated. The frequency of variables was expressed as proportions and analysed.

**Results:** The mean age of males was 62 and females 59 appropriately. The male/female ratio of Multiple myeloma was found to be 1.6:1. The associated neurological symptoms were root pain for 14.3% of patients. Almost 8.6% had paraparesis and 2.9% were suffering from paraplegia and 1.4% had quadriplegia, paraesthesia, bulging right eye and diplopia. Anemia was found in 87.1% and ESR was raised above 30 in 92.8% of patients. The total count more than Eleven thousand was found for 10% and less than four thousand for 1.4% of patients. Eosinophilia was seen among 7.1%, 1.4% of patients had Peripheral smear >10% and Electrophoresis M band was seen in 78.6% of patients. Lytic lesions on X-Ray Skull neck were found in 62.9% and X Ray Spine were found in 1.4% of patients.

**Conclusion:** 70 cases detected at a tertiary Medical College at Northern Kerala in a year indicate significant incidence of the disease. Professional Medical Associations should give importance to this topic and case studies of Multiple Myeloma should be included in medical conferences to raise the competence of doctors regarding the disease.

**Keywords:** Multiple Myeloma, Northern Kerala.

### Introduction

Malignant proliferation of plasma cells derived from a single clone is termed as Multiple Myeloma. The Plasma cell dyscrasias is broad heading which include this type of diseases. Multiple myeloma is the second most common hematological malignancy after non hodgkins lymphoma and it accounts for 15% of all hematological malignancies. The incidence of this disease increases with age in a spectrum of 4/lac in the general population to around 30/lac in over 25 years population. Even though lots of advancements have been made in the pathogenesis and etiology of this disease, it has still not made its way into the category of curable diseases.<sup>1</sup>

Egyptian mummies showed light to describe diseases which were similar to Multiple myeloma. In 1844, Samuel Solley reported a case of myeloma in Sarah Newbury. He described it as "mollitis ossium". Together with Bence Jones; he found that the urine analysis of the patient showed a protein with the heat properties often observed for urinary light chains. It later on came to be known as the Bence Jones Protein. MacIntyre and Dalrymple described the properties of the affected bone in the same patient and MacIntyre called it Mollitis and Fragillitis ossium.<sup>2,3</sup>

As per the GLOBOCAN/IARC data, the worldwide Age Standardized Rate (ASR) for incidence of MM is 1.4/1,00,000 population accounts to 1,00,000 new cases every year. In the US as per the SEER data, the ASR for incidence is higher at 5.8/1, 00,000 population accounting for 21,000 new cases each year. Worldwide the 5 year prevalence of the disease is 2, 10, 697 or 4.3/1, 00,000

population. The ASR for MM incidence in India is 0.7/1, 00,000 population amounting to about 6,800 new cases a year.<sup>4-6</sup>

Present clinical research focuses on the balance between treatment efficacy and quality of life, the optimum sequencing of treatment options, the question of long-term remission and potential cure by multimodal treatment, the pre-emptive treatment of high-risk smoldering myeloma, and the role of maintenance. Upcoming results of ongoing clinical trials, together with a pipeline of promising new treatments, raise the hope for continuous improvements in the prognosis of patients with myeloma in the future.<sup>7</sup> The introduction of high-dose melphalan with autologous stem-cell transplantation and the availability of molecular-targeted novel agents such as immune-modulatory drugs and proteasome inhibitors have dramatically changed the treatment strategies for MM. Achievement of a high response rate resulted in the extension of overall survival, but further research and the development of more multimodality therapeutic approaches is warranted to cure this disease.<sup>8</sup>

The reclassification of a subset of patients with smoldering MM, based on high-risk biomarkers, and the development of the revised international staging system are among the key new developments in diagnosis and staging.<sup>9</sup> Compared with MM patients diagnosed in earlier years, those diagnosed after 2010 had higher rates of novel therapy use and better survival outcomes; patients diagnosed in 2012 were 1.25 times more likely to survive 2 years than those diagnosed in 2006.<sup>10</sup>

The disease diagnosis is quite difficult and thereby patients get diagnosed very late moving to complications and late stage of the disease. This study is an attempt to study the profile of Multiple myeloma of Northern Kerala as there are only few studies from this part of the country.

**Materials and Methods**

Seventy patients of multiple myeloma admitted to the Oncology department and department of Medicine at Government Medical College Hospital Calicut were studied for duration of six months. The data was collected using convenient sampling method. It was an observational study with an objective to look into clinical profile of multiple myeloma. All the new cases of multiple myeloma admitted to the department of medicine and Department of Medicine at Government Medical College Hospital Calicut were included in the study. The diagnosis of multiple myeloma was based on the following staging.<sup>11</sup>

**Diagnosis of Multiple Myeloma**

**Major Criteria**

1. I = Plasmacytoma on tissue biopsy
2. II = Bone marrow with greater than 30% plasma cells
3. III = Monoclonal globulin spike on serum protein electrophoresis, with an immunoglobulin G (IgG) peak of greater than 3.5 g/dL or an immunoglobulin A (IgA) peak of greater than 2g/dL, or urine protein electrophoresis (in the presence of amyloidosis) result of greater than 1 g/24 h.

**Minor Criteria**

- a = Bone marrow with 10-30% plasma cells
- b = Monoclonal globulin spike present but less than category III
- c = Lytic bone lesions
- d = Residual normal immunoglobulin M (IgM) level of less than 50mg/dL, IgA level of less than 100 mg/dL, or IgG level of less than 600 mg/dL

The following combinations of findings are used to make the diagnosis:

- I plus b
- I plus c
- 19
- I plus d

- II plus b
- II plus c
- II plus d
- III plus a
- III plus c
- III plus d
- a plus b plus c or a plus b plus d

The inclusion criteria included increased numbers of abnormal, atypical or immature plasma cells in the bone marrow or histological proof of plasmacytoma, presence of an M-protein in the serum or urine, bone lesions consistent with those of multiple myeloma. The exclusion criteria were Monoclonal gammopathy of undetermined significance (MGUS), smoldering multiple myeloma, solitary plasmacytoma, plasma cell leukemia. All the 70 patients were subjected to detailed history taking and meticulous clinical examination. Laboratory work up – Biochemical work up included urine Bencejones done with the heat coagulation method, serum albumin, calcium, uric acid done using standard biochemical kits. Serum immune electrophoresis was done using the agar gel electrophoretic method. Complete hemogram and bone marrow aspiration studies were done. They were analysed by the Pathologist at the department of Pathology Calicut Medical College. Skeletal survey – X-ray skull PA and lateral view, X-ray pelvis PA and lateral view, X-ray cervical, thoracic, lumbar spine PA and lateral view, chest X-ray PA and lateral view, X-ray humerus PA and lateral view, X-ray hip and femur PA and lateral view was done in all patients. All the data was entered into excel and transferred to Spss version 16. The data was expressed in frequency and depicted with appropriate tables and graphs.

**Results**

Multiple Myeloma cases comprises of 43 males and 27 females. Most of them (60%) belongs to 51 to 70 age group. The mean age of males were 62 and females were 59.

Body and bone pain were the complains for majority (68.6%) of the patients followed by loss of appetite, loss of weight, fever, low back ache, bleeding manifestation, cough, chest pain, constipation, vomiting, pain abdomen, bleeding, edema, oliguria, dysurea, purulent discharge nose, thirst.

**Table 1**

Symptoms	Male		Female		Total	
	Number	%	Number	%	Number	%
Bone pain	31	72.1	17	63	48	68.6
Body pain	31	72.1	17	63	48	68.6
Fever	12	27.9	7	25.9	19	27.1
Bleeding Manifestation	4	9.3	2	7.4	6	8.6
Odema	2	4.7	0	0	2	2.9
Oliguria	2	4.7	0	0	2	2.9

Table 2

	Number	Percentage
<b>Anemia</b>	61	87.1
<b>ESR</b>	65	92.8
<b>Total Count</b>		
<4000	1	1.4
>11000	7	10
Easnophilia	5	7.1
<b>Peripheral Smear-Plasma &gt;10%</b>	1	1.4
<b>M Band</b>	55	78.6
<b>X Ray – Skull neck</b>	44	62.9
<b>X Ray – Skull Spine</b>	1	1.4

The associated neurological symptoms were root pain for 14.3%. 8.6% had paraparesis and 2.9% were suffering from paraplegia. 1.4% had quadriplegia, paraesthesia, buldging right eye and diplopia. The signs elicited were pallor for 84.3% and 27.1% patients had increase in temperature. Bleeding manifestation was found out in 8.6%. Clubbing, Lymphadenopathy and oral candidiasis was seen for 1.4%. Spine tenderness was elicited for 32.9%. Rib tenderness was there for 8.6%. Swellings were seen for 7.1% and pelvic tenderness for 5.1%.

Anemia was found in 87.1% and ESR was raised above 30 in 92.8%. The total Count more than Eleven thousand was found for 10% and less than four thousand for 1.4%. Easnophilia was seen among 7.1% and 1.4% patients had Peripheral smear >10%. Electrophoresis M band was seen in 78.6%. X- Ray Skull neck lytic lesions were found in 62.9% and X-Ray Skull Spine lytic lesions were found in 1.4%.

## Discussion

The male/female ratio of Multiple myeloma is 1.4:1 and mean 5-year survival rate of 33%.<sup>12</sup> In our study Multiple Myeloma cases comprises of 43 males and 27 females and most of them (60%) belongs to 51 to 70 age group and male/female ratio of Multiple myeloma is 1.6:1. The mean age of males were 62 and females were 59. A study conducted by Fousad et al<sup>13</sup> found male to female ratio was 1.3:1. Mean age of the patients in the study population was 62 years. Diwan et al<sup>14</sup> found that out of total 20 patients, 10 were males and 10 were females with sixth decade as the common age group at presentation. 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. Mean age of the patients in the study population was 62 years and one patient was above 70 years of age.

Fousad et al<sup>13</sup> found that 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. Diwan et al<sup>14</sup> found common clinical symptoms were bone pains, localized body swelling, fever, generalized weakness and fatigue and motor weakness of lower limbs. Clinical examination revealed

pallor in 80% patients, bony tenderness in 85% patients and 55% patients presented with infections.

Majority 29 (90.6%) of patients had normal white blood cell count, 2 (6.3%) of them had leukocytosis and 1 (3.1%) had leucopenia. Five (15.6%) cases had thrombocytopenia.

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% ± 19.97% in Fousad et al<sup>13</sup> study. Diwan et al<sup>14</sup> found Hematological features were anemia in all (100%), median Hb concentration was 9.34 g/dL and elevated ESR was present in all (100%) cases. Rouleaux formation was observed in 7 patients (35%) at presentation white blood cells count was less than 6000 in 4 patients (20%) and platelet count was less than 1 lakh/mm<sup>3</sup> in 2 patients (10%) and greater than 4 lakh in 1 patient (5%). Serum creatinine of more than 1.9 mg/dL was seen in 6 patients (30%) at presentation. Hypercalcemia was observed in one patient (5%). All patients had a presence of M band on serum protein electrophoresis, whereas 30% patients had urinary Bence Jones protein positive.

According to Diwan et al (14) 29 (91%) of 32 had lytic lesions in the skull. All patients in study group (100%) had the presence of M band on serum protein electrophoresis and  $\gamma$ -region was the most frequent location of the monoclonal band. 6 patients (30%) had urinary Bence Jones protein. Among skeletal involvement, 19 patients (85%) had osteolytic lesions, 8 patients (40%) had generalized osteoporosis, 7 patients (35%) had pathological fractures. Spine and skull were the common sites of involvement 60% and 55% respectively. One patient did not have skeletal involvement. Bone marrow examination revealed the presence of more than 50% plasma cells in 9 cases (45%), 7 patients (35%) had 10-30% plasma cells 4 patients (20%) had plasma cells in the range of 30-50%. 27 (84%) had lytic lesions in the spine.<sup>11</sup> According to diwan et al,<sup>14</sup> Hematological features were anemia in all (100%), median Hb concentration was 9.34 g/dL and elevated ESR was present in all (100%) cases. Rouleaux formation was observed in 7 patients (35%) at presentation white blood cells count was less than 6000 in 4 patients (20%) and

platelet count was less than 1 lakh/mm<sup>3</sup> in 2 patients (10%) and greater than 4 lakh in 1 patient (5%). Serum creatinine of more than 1.9 mg/dL was seen in 6 patients (30%) at presentation. Hypercalcemia was observed in one patient (5%). All patients in study group (100%) had the presence of M band on serum protein electrophoresis and  $\gamma$ -region was the most frequent location of the monoclonal band. 6 patients (30%) had urinary Bence Jones protein. Among skeletal involvement, 19 patients (85%) had osteolytic lesions, 8 patients (40%) had generalized osteoporosis, 7 patients (35%) had pathological fractures. Spine and skull were the common sites of involvement 60% and 55% respectively. One patient did not have skeletal involvement. Bone marrow examination revealed the presence of more than 50% plasma cells in 9 cases (45%), 7 patients (35%) had 10-30% plasma cells 4 patients (20%) had plasma cells in the range of 30-50%. 50% patients had fractures, may be due to delayed presentation by the patients and late diagnosis by attending physicians.

### Conclusion

Multiple myeloma is a well reported entity in the medical literature from western world. The fact that 70 cases detected in one year indicate significant incidence of the disease in Northern Kerala. No definite predisposing factors could be made out. Male female ratio is 1.6:1 is noted. Bone pain and body pain are the most common symptoms. Anemia is present in all cases. ESR is increased in 95% patients. Hypercalcemia was seen only 2.5% and almost 50% had fractures. The physician should be able to think probable diagnosis as multiple myeloma and treat earlier to prevent fractures. Continuing Medical Education should incorporate topics and case studies of Multiple Myeloma to empower diagnosing capacity of physicians.

**Conflict of Interest:** None.

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