

# CLINICAL PROFILE OF MULTIPLE MYELOMA IN A TERTIARY CARE HOSPITAL OF PESHAWAR, PAKISTAN

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## ABSTRACT

**OBJECTIVE:** To determine demographic and clinico-pathological characteristics of patients suffering from multiple myeloma (MM) in Peshawar, Pakistan.

**METHODS:** This descriptive, retrospective study was conducted at Pathology Department, Rehman Medical Institute, Peshawar, Pakistan from January 2006 to September 2018. Detailed information of forty patients diagnosed with MM was collected. World Health Organization (WHO) set criterion was utilized to diagnose MM. SPSS version 22 was used for Statistical analysis.

**RESULTS:** Out of 40 patients, 72.5% were males with male to female ratio of 2.63:1 and mean age of patients was  $59.26 \pm 13.1$  years. The common presenting complaints were body/bony pain (87.5%), fatigue (72.5%), body tenderness (45%) and backache (42.5%). Pallor was present in 33 (82.5%) patients. Laboratory studies showed mean hemoglobin level of  $8.6 \pm 2.1$  g/dl, anemia (92.5%), thrombocytopenia (27.5%) and hypercalcemia (17.5%). Elevated ESR  $> 100$  was noted in 29 (72.5%) cases. Renal impairment was established in 35% of patients. Urinary Bence Jones protein was present in 13 (32.5%). Serum protein electrophoresis showed M band in 39 (97.5%) cases. Lytic lesions were detected in X-rays of 31 (77.5%) patients. Based on international staging system, nine (22.5%) cases were in stage I, 16 (40%) in stage II and 15 (37.5%) in stage III.

**CONCLUSION:** Majority of multiple myeloma patients in our study were in the 6<sup>th</sup> decade of life. Bone pain and fatigue were the most common presenting symptoms. Anemia and elevated ESR were the most common laboratory parameter. Most of the patients were diagnosed in later stages (stage II and III).

**KEY WORDS:** Multiple Myeloma (MeSH); Anemia (MeSH); Renal impairment (Non-MeSH); Kidney Diseases (MeSH); Hypercalcemia (MeSH); Thrombocytopenia (MeSH); Hypoalbuminemia (MeSH); Bone Marrow (MeSH); Myeloma Proteins (MeSH).

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## INTRODUCTION

Plasma cell dyscrasias are a group of concomitant derangements causing an abnormally up heaved number of monoclonal plasma cells and documented by the presence of monoclonal immunoglobulin in the blood also known as M-protein.<sup>1</sup> Multiple myeloma (MM) is the utmost noteworthy and prevent disorder among all plasma cell dyscrasias.<sup>2</sup> After lymphomas, MM contributes for 1.3%

of all cancer combined and 15% of blood-related malignancies. MM is predicted to be the second most ubiquitous blood cancer.<sup>3</sup> Among Asian countries an expeditious elevation in the incidence of multiple myeloma has been noted causing a great disturbance in the health care system of these countries.<sup>4</sup>

In the United States, MM contributes to approximately 1-2% of all malignancies and round about 17% of hematological neoplasm. The yearly occurrence of

MM in the US is approximately 4-5/100,000.<sup>5</sup> Alike occurrence has been reported in the UK and in Europe.<sup>6</sup> Worldwide, about 154,000 cases and 101,000 deaths per year is attributed to MM.<sup>7</sup> There is an exaggeration in incidence with age and the average age of diagnosis is revealed to be 65-70 years. MM is more prevalent in males as compared to females.<sup>8</sup> There are some genetic and environmental considerations that have been suspected in the etiology and pathogenesis of MM, peculiarly pesticides, radiations and certain chemicals like benzene, asbestos and arsenic.<sup>9</sup> MM is presented clinically with exalted serum calcium, lytic lesions of bone and anemia.<sup>10</sup> The myeloma cells cause an increase in the activity of osteoclasts by releasing certain cytokines which eventually leads to the clinical manifestations such as lytic lesion of the bones, hypercalcemia and ultimately causing pathological fractures.<sup>11</sup>

As not much data is available regarding the clinical course or the demographic diversity of MM in Pakistan, this study was planned to determine demographic and clinic-pathological features of patients with multiple myeloma in our setup.

## METHODS

This descriptive retrospective study was brought about at Pathology Department, Rehman Medical Institute, Peshawar, Pakistan from January 2006 to September 2018. Data of forty patients diagnosed with MM were evaluated. World Health Organization (WHO) criterion was opted for the diagnosis of MM.<sup>12</sup> Diagnosis required meeting three criteria includes:

- i). Detection of M-protein in serum or urine.
- ii). Bone marrow clonal plasma cells.

**TABLE I: CLINICOPATHOLOGICAL FEATURES OF PATIENTS (n=40)**

Characteristics	Frequency	Percentage	
Age Groups (years)	40-50	16	40
	51-60	14	35
	61-70	7	17.5
	>70	3	7.5
Gender	Male	29	72.5
	Female	11	27.5
Symptoms & Signs	Bone and body pain	35	87.5
	Pallor	33	82.5
	Fatigue	29	72.5
	Fever	18	45
	Body tenderness	18	45
	Back pain	16	42.5
	Constipation	13	32.5
	Weight loss	11	27.5
	Nausea and vomiting	9	22.5
	Neurologic deficit	7	17.5

**TABLE II: LABORATORY PARAMETERS OF PATIENTS (n=40)**

Parameters	Frequency	Percentage
Anaemia (<12 g/dl)	37	92.5
Thrombocytopenia (<150x10 <sup>9</sup> /L)	11	27.5
Elevated ESR (>100)	29	72.5
Hypercalcaemia (>11 mg/dl)	7	17.5
Elevated serum creatinine level (2 mg/dl)	14	35
Hypoalbuminemia (<3.5 g/dl)	27	67.5
High LDH level (>450 IU/L)	17	42.5
Urinary Bence Jones protein	13	32.5
M band on Serum protein electrophoresis	39	97.5
X-ray lytic lesions	31	77.5

iii). Related organ or tissue impairment.

A detailed history included name, age, contact details, sex, occupation, marital status, education, and symptoms of MM patients were recorded. 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 and a skeletal survey were retrieved from patient record. Ethical approval was taken from the Ethical committee of Rehman Medical College, Peshawar.

SPSS version 22 was used to carry out statistical analysis. Categorical quantitative data was presented in terms of frequencies and percentages.

Mean and the standard deviation were reported for numerical quantitative variables.

## RESULTS

During our study period, 40 patients were found to have MM, in which 29 (72.5%) were male and rest were females, with male to female ratio of 2.63:1.

Age range was from 40-81 years, with a mean age of 59.26±13.1 years. The common presenting complaints included body and bone pain in 35 (87.5%) followed by fatigue in 29 (72.5%) patients rest clinical characteristics are summarized in Table I.

Laboratory studies showed anemia (Hb <12g/dl) in 37 (92.5%) patients, with a mean hemoglobin level of 8.6±2.1 g/dl.

Severe anemia was seen in 14(35%) patients with hemoglobin less than 7 gm/dL, 21(52.5%) had moderate anemia with a hemoglobin level between 7 to 10 gm/dL and 5(12.5%) had mild anemia with a hemoglobin level between 10 to 12 gm/dL. Thrombocytopenia (platelets <150) were detected in 11(27.5%) with mean platelets count of 173±149x10<sup>9</sup>/L. Other laboratory characteristics are summarized in Table II.

Bone marrow examination uncloned, nine (22.5%) cases had bone marrow plasma cell concentration of <20%, 7 (17.5%) between 20% -30%, 12 (30%) between 30%- 40%, 7 (17.5%) between 40% to 50% and 5 (12.5%) cases >50%. The mean bone marrow plasma cell concentration was 34%. Based on international staging system (ISS), nine (22.5%) cases were found to be in stage I, 16 (40%) were found to be in stage II and 15 (37.5%) were in stage III.

## DISCUSSION

Multiple myelomas (MM) are characterized by the cancerous propagation of plasma cells creating a monoclonal immunoglobulin. MM usually evolve in advance ages and majority after the 6<sup>th</sup> decade involving mostly males. In our study age group was ranged from 40-81 years, with the mean age of 59.26±13.1 years. It corresponds to findings of other local studies with mean age of 59 and 61 years.<sup>13,14</sup> Similar study from India reported with a mean age of 58.8 years.<sup>15</sup> however, the median age of MM is high in developed countries with a median age of 72-74 years.<sup>16</sup> Environmental and genetics fluctuation could be the cause of between different part of the world.

Majority of patients in our study presented with bone and body aches (87.5%) and were pale (82.5%). Bone pain was markedly felt in chest or back and sometimes involving extremities, which in most cases (60%) was present at the time of diagnosis. The pain does not appear at night except with a change of posture and is mostly initiated by movement. Reduction in patient's height is noticed by several inches

because of vertebral collapse. There are plasmacytomas of ribs and present as expanding costal lesions or soft tissue masses.<sup>1</sup>

In our study, 92.5% of patients had anemia, which contributes frequently to weakness and fatigability. According to Kaur P, et al.<sup>17</sup> anemia is the most frequent clinical manifestation of MM, around 88% showed hemoglobin below 12mg/dl.<sup>17</sup> In another study by Kyle RA, et al.<sup>1</sup> it was reported that normocytic normochromic anemia was present in 73% at the time of diagnosis while in 97% somewhere during the course of the disease.<sup>1</sup> This anemia can be analogous to renal derangement, replacement of bone marrow or can be because of dilution in the case of huge M-protein.

Bone marrow infiltration by myeloma cells can cause thrombocytopenia and be noticed in 15.6% cases as in previous studies.<sup>17</sup> Hypercalcemia contemplated as one among the significant diagnostic criteria and was observed in just 17.5% patients. Hypercalcemia according to Kyle RA, et al.<sup>1</sup> is found in 28% of one series of patients suffering from MM at the time of diagnosis; serum calcium was  $\geq 11$  mg/dL in 13% and can require emergent treatment. Binding of the monoclonal protein with calcium may be due to the rise in serum calcium.

In our study renal impairment was found in 35% of patients, in most one half of the patient's serum creatinine concentration was raised at the time of diagnosis and is  $>2$ mg/dl; in MM renal failure may be the presenting manifestation.<sup>18</sup> Myeloma Kidney or hypercalcemia can be important cause of renal failure in MM.

In majority, low serum albumin was found to be 67.5%, the basis for a three-stage international staging system that anticipates survival is formed by the combination of serum  $\beta_2$  and albumin. In previous studies for determining disease severity in symptomatic MM, serum albumin level was found to be an important factor.<sup>8</sup> On serum protein electrophoresis, 97.5% of patients have an M band and gamma globin region which was the most common site. The majority (97%) of patients with MM will have a monoclonal protein produced

and secreted by the malignant plasma cells, which can be revealed by protein electrophoresis of serum (SPEP) and of urine aliquot (UPEP) from a 24-hour collection combined with immunofixation of the serum and urine.<sup>1</sup>

In the majority of patients, bone marrow constitutes 10% or even more clonal plasma cells, because of patchy bone marrow involvement, bone marrow aspiration and biopsy may reveal plasma cell below 10% in roughly 4% of patients. For example, a study by Mayo Clinic, plasma cells constituted more than 10% of all nucleated cells in 96% of patients but this value ranged from less than 5 percent to almost 100 percent, with a median value of 50%.<sup>1</sup>

## CONCLUSION

Majority of multiple myeloma patients in our study were in the 6<sup>th</sup> decade of life but a few younger age groups were also involved. Bone pain along with fatigue were the most common presenting symptoms. Anemia and elevated ESR were the most common laboratory parameter. Most of the patients were diagnosed in later stages (stage II and III).

## LIMITATIONS

This was a retrospective study and relatively small sample study and its findings cannot be generalized.

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### AUTHORS' CONTRIBUTIONS

Following authors have made substantial contributions to the manuscript as under:

**SB:** Concept & study design, acquisition of data, drafting the manuscript, final approval of the version to be published

**ZB:** Acquisition, analysis & interpretation of data, critical review, final approval of the version to be published

**NA:** Acquisition, analysis & interpretation of data, final approval of the version to be published

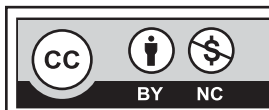
*Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.*

### CONFLICT OF INTEREST

Authors declared no conflict of interest

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