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An Analysis of the Clinical and Laboratory Profiles of Patients Diagnosed with Multiple Myeloma in a Tertiary Care Hospital

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ABSTRACT

Background and aim: Multiple myeloma (MM) is a plasma cell neoplasm characterized by the proliferation of terminally differentiated B lymphoid cells, producing monoclonal antibodies and significant end-organ damage. It is the second most common hematological malignancy after lymphoma, resulting in considerable morbidity and mortality. This study aimed to explore MM's clinical and laboratory characteristics in a specific region with limited resource settings, emphasizing the importance of early detection and intervention.

Material and methods: The present study was performed from January 2019 to June 2022 in a tertiary healthcare facility. A detailed clinical history was recorded. Various laboratory parameters were assessed. Diagnosis was established using the criteria provided by the International Myeloma Working Group (IMWG) and the World Health Organization (WHO). The staging of the patients was conducted according to the Durie-Salmon staging system and CRAB criteria. Prognostic factors were assessed using the ISS system.

Results: Fifty-four newly diagnosed cases were studied. The results reinforced that MM primarily affects the middle-aged and elderly, particularly males. Common clinical presentations included generalized weakness, pallor, and renal dysfunction, while anemia and thrombocytopenia were frequently observed. Bone marrow analysis revealed a high percentage of plasma cells, with most cases categorized as Durie-Salmon stage III.

Conclusions: This research contributes to a better understanding of MM's clinical and laboratory characteristics. Further research and collaborative efforts involving larger cohorts and current staging systems are recommended for deeper insights into this complex hematological malignancy, ultimately improving patient care and outcomes.

1. Introduction

Multiple myeloma (MM) is a plasma cell neoplasm characterized by clonal proliferation of terminally differentiated B lymphoid cells resulting in monoclonal antibodies and end-organ damage.[1, 2] End organ dysfunction includes hypercalcemia, renal insufficiency, anemia, and bone destruction, collectively referred to as the CRAB criteria. It accounts for 1% of all malignant tumors, 10-15% of all hematological malignancies, and 20% of deaths from hematological malignancies. It is a disease of the elderly, with a median age of presentation around 60-70 years. The incidence increases with age, being more prevalent in males.[3] The etiology of the disease is unknown. Environmental, occupational, radiation exposure, benzene exposure, metal industries, and pre-existing conditions were found to increase the incidence of MM.[4] Incidence is higher in high-income countries than in Asia and sub-Saharan Africa, possibly because of variations in diagnosis.[5] In contrast to Western countries, India demonstrates a comparatively lower median age of presentation, ranging from 55 to 62 years.[6-9] There was a 126% increase in the global incidence of MM owing to population growth, an aging world population, and increased age-specific incidence rates from 1990 to 2016.[5] The clinical features are due to marrow infiltration by plasma cells and secretion of M proteins. Clinical findings, laboratory investigations, radiological parameters, bone marrow examination, serum electrophoresis, and free light chain assay help diagnose MM. Plasma cell percentage, morphology, and pattern of infiltration in the bone marrow examination have an essential role in correlation with the clinical stage and survival. The old criteria used for diagnosis were as per Salmon and Durie staging. The International Myeloma Working Group (IMWG) in 2014 revised the criteria for diagnosis of various plasma cell neoplasms. The International Staging System (ISS) is based on serum β2 microglobulin and serum albumin, which is used to evaluate tumor burden and prognosis.[10] In 2015, Palumbo et al. published a Revised International Staging System (RISS), which combined ISS with chromosomal abnormalities (CA) and lactate dehydrogenase (LDH).[11] Currently, the primary treatment approach for myeloma consists of

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proteasome inhibitors and immunomodulatory drugs. Steroids, specifically dexamethasone or prednisolone, are often included in treatment regimens.

2. Material and methods

Patient selection

The study was initiated after approval from the institutional ethical and scientific committees (MGMC&H/IEC/JPR/2021/344, dated 12/03/2021). The study included all newly diagnosed cases of MM between January 2019 and June 2022, resulting in a total of 54 MM patients participating in the study. We included patients who were above 18 years of age and diagnosed with multiple myeloma, as well as patients who provided informed consent. We excluded patients with multiple myeloma associated with other hematological malignancies and patients lost to follow-up.

Methodology

This study reviewed and analyzed 54 cases of newly diagnosed MM patients from January 2019 to June 2022. We retrieved the case files from medical records and analyzed the laboratory data from the electronic health records of our hospital. Informed consent was obtained from all patients included in the study. Patients who fulfilled the diagnostic criteria for MM from the onset of the disease to the last follow-up or until death were retrospectively analyzed. A spreadsheet was created, which consisted of the patient's clinical details and their laboratory investigations. A detailed clinical history was recorded, including presenting symptoms, duration of symptoms, and demographic profile of the patient. Radiological investigations were assessed for bony changes. Various laboratory parameters were evaluated, including complete blood count (hemoglobin for anemia, platelet counts for thrombocytopenia, total leukocyte counts), renal function tests (blood urea, serum creatinine), liver function tests, serum total protein, serum albumin, and globulin, A/G ratio, LDH, and serum calcium. Geimsa-stained peripheral smears were examined for red cell morphology, differential leukocyte count, and platelet count. Peripheral blood films show characteristic increased background staining with rouleaux formation, normocytic normochromic red cells, and occasional circulating plasma cells. All patients were assessed for myeloma-specific parameters, including bone marrow aspiration, bone marrow biopsy, serum protein electrophoresis (quantification of M band/ M-protein), immunofixation, serum free light chains (kappa and lambda), qualitative and quantitative estimation of serum beta-2 microglobulins, and urinary Bence Jones protein. The diagnosis of multiple myeloma was established using the criteria provided by the International Myeloma Working Group (IMWG), which has been adopted by the World Health Organization (WHO). Staging of the patients was conducted according to the Durie-Salmon staging system and CRAB criteria (C-hypercalcemia, R-renal dysfunction, A-anemia, and B-skeletal survey for bony lesions). Follow-up and survival analysis were performed from diagnosis up to 6 months. Prognostic factors were assessed using the ISS, which quantitatively estimated serum albumin, serum β2 microglobulin, and serum LDH. However, the study did not include fluorescence in situ hybridization (FISH) analysis, which prevented the staging according to the RISS.

Statistical analysis

Descriptive statistics such as mean/median/range were calculated for all the variables.

3. Results

Fifty-four newly diagnosed MM patients were included in this study, of which 34 were males (62.96%). At the same time, 20 were females (37.04%), resulting in a male-to-female ratio of 1.7:1. The average age of patients at presentation was 61.40 years (range 40-84 years). The most commonly observed clinical presentation was generalized weakness followed by pallor, renal dysfunction, and fever. (Table 1). The baseline laboratory characteristics are presented in Table 2. In our study, most patients (74%) displayed anemia, while only 18.52% had thrombocytopenia.

Table 1. Clinical presentation of patients with Multiple Myeloma.

Clinical Features	No of Patients (n-54)	Percentage
Generalized weakness	34	62.96
Pallor	29	53.70
Renal dysfunction, Hyperuricemia, Acute Kidney Injury	21	38.88
Fever/ PUO	10	18.52
Back pain	9	16.67
Generalized bone pain	6	11.11
Pathological fracture	5	9.26
Shortness of breath	3	5.55
Deafness	1	1.85
Hepato-splenomegaly	1	1.85
Pedal edema	1	1.85
Paravertebral mass	1	1.85
Limb weakness	1	1.85

Table 2. Laboratory characteristics of patients with Multiple Myeloma.

Variables	Value	Number of Patients (%)	Mean of Variable
Hemoglobin (gm/dl)	<10	40 (74.07%)	8.48 gm/dl
	>10.1	14 (25.93%)	
Platelet counts (x 10^9/L)	<120 (Thrombocytopenia)	10 (18.52%)	169.66 x 10^9/L
	≥120	44 (81.48%)	
Rouleaux formation	Seen	35 (64.81)	-----
	Not seen	19(35.19)	
Serum Albumin (gm/dl)	<3.5 (Low)	34 (62.96%)	3.17 gm/dl
	3.5-5	20 (37.04%)	
Serum LDH (IU/L)	<120	1 (1.85%)	219.07 IU/L
	120-246	34 (62.96%)	
	>246	19 (35.19%)	
Serum calcium (mg/dl)	<10.2	13 (24.07%)	9.57 mg/dl
	≥10.2	41 (75.93%)	
Serum creatinine (mg/dl)	<1.25	20 (37.04 %)	2.35 mg/dl
	>1.25	34 (62.96 %)	
Serum β2 microglobulin (mg/L)	High	53 (98.15)	-----
	Normal (0.67-2.1 mg/L)	1 (1.85)	
Bence Jones proteins	Positive	30 (55.56)	-----
	Negative	24 (44.44)	

Analysis of bone marrow aspiration revealed that 28 patients (51.85%) had plasma cell percentages ranging from 20% to 50%, 22 patients (40.74%) had percentages greater than 50%, and 4 patients (7.41%) had less than 20% plasma cells. The findings from bone marrow biopsy were consistent with the results of the aspiration studies, showing sheets of plasma cells in 53 patients (98.15%). The M-band (monoclonal protein band) was detected on serum electrophoresis in 85.1% of cases. On Immunofixation analysis, IgG antibody was identified in 45 patients (83.33%), while IgA antibody was detected in

two patients (3.7%). The serum-free light chain (SFLC) assay demonstrated elevated levels of kappa-free light chains in 47 patients (87.04%) and lambda-free light chains in 22 patients (40.74%), with the kappa/lambda (K/L) ratio being higher in 40 patients (74.07%). Table 3 shows the diagnostic and staging criteria used in our study including the CRAB criteria, ISS, and Durie-Salmon staging system.(Table 3) All the patients included in this study were followed up for six months, and no mortality was observed during this time.

Table 3. Diagnostic and Staging criteria in Multiple Myeloma.

Diagnostic and Staging Criteria				
CRAB criteria	C-Hypercalcemia (S. Calcium >10.2 mg/dL)			13 (24.07%)
	Renal dysfunction (S. Creatinine > 1.25mg/dL)			34 (62.96%)
	Anemia (Hb < 10 %)			40 (74.07%)
	Bone lesions on skeletal survey			5 (9.26%)
International Staging System (ISS)		**Stage I**	**Stage II**	**Stage III**
	Sr. Albumin (gm/dl)	>3.5 n-34, 62.96%	<3.5 n-20, 37.04%	N/A
	Sr. β2 microglobulin (mg/L)	<3.5 n-1, 1.85%	3.5-5.5 n-32, 59.25%	>5.5 n-21, 38.88%
Durie-Salmon staging system	Stage-I			n-13; 24.07 %
	Stage-II			n-4; 7.4%
	Stage-III			n-37; 68.51%

4. Discussion

Multiple myeloma is a disease resulting from B cell neoplastic proliferation in bone marrow. The present study comprised a cohort of 54 patients with an average age of 61.4 years and a higher prevalence in males, concordance with similar studies.[7, 12-14] The clinical presentation of patients with MM varies, with generalized weakness, bone pains, and pallor as the leading symptoms. The most common clinical presentation in our study was generalized weakness and pallor, which were consistently observed in various studies.[12, 15, 16] Bone pains were the least common presentation in our study. This finding is discordant with similar studies where bone pain was the most common symptom.[7, 13, 14, 17-20] (Table 4)

Table 4. Comparison of demographic profile and clinical characteristics of patients with published studies.

Studies	Number of Patients	Mean Age (Years)	Male: Female Ratio	Clinical Features
Kyle RA et al., 2003[14]	1027	66	1.4:1	Bone pain (58%), Generalized weakness/ Fatigue (32%), Fever 0.7%
Kaur P et al., 2014[7]	28	58.8	1.5:1	Bone pain (50%), Generalized weakness/ Fatigue (46.4%)
Sultan S et al., 2016[15]	61	56.1±12.8	2:1	Generalized weakness/Fatigue (81.9%), Backache (80.3%), Bone pain (67.2%), Pallor (44.2%)
Pegu AK et al., 2016[12]	44	57.7	1.6:1	Backache (86%), Pallor (84%), Generalized weakness/ fatigue (80%), Bone pain (77%), Paraplegia (32%), Fever (32%)
Shin J et al., 2017[17]	32	37	1.46:1	Bone pain (45%), Pallor (29%)
Kaushik R et al., 2017[19]	51	58.38	1.42:1	Bone pain (62.74%), Generalized weakness (23.52%), Fever (15.68%), Renal dysfunction (15.68%)
Jakhetia H et al., 2019[18]	30	52	1.72:1	Bone pain (83%), Generalized weakness (73%), Backache (60%), Pallor (53%), and Pathological fracture (40%)
Sheik N et al., 2019[20]	26	60	1.3:1	Fever (50%), Bone pain (42%), Generalized weakness (42%)
Sharma S et al., 2020[13]	37	64.65	3.1:1	Bone pain, Pallor, Backache
Mishra D et al., 2021[16]	49	59.08	1.6:1	Pallor (80%), Generalized weakness (53%), Backache (51%), Bone pain (29%), Fever (27%)
Present study	54	61.4	1.7:1	Generalized weakness (62.96%), Pallor (53.7%), Renal dysfunction (38.88%), Fever (18.52%), Backache (16.67%), Bone pain (11.1%)

The most common hematological manifestations of anemia and thrombocytopenia occur primarily due to the infiltration of neoplastic plasma cells in bone marrow. In our study, we observed the presence of anemia in 74.07%, while thrombocytopenia was detected in 18.52% of the cases. Peripheral blood films showed rouleaux formation in 64.08% of the cases, which falls within the range reported in previous studies.[7, 18, 20] Hypercalcemia is the most prevalent metabolic complication of MM and was observed in 76% of patients in our study. We observed a higher incidence of hypercalcemia compared to earlier research, which could be attributed to late presentation in the course of the disease as our institute serves as a tertiary care referral hospital in our state.[7, 12-20] Patients with myeloma-related hypercalcemia typically exhibit compromised renal function in nearly all cases, as was the case in our study. Hypoalbuminemia is primarily linked to the extent of myeloma proliferation and higher stage of disease, as was found in 62.96% of our cases. Serum LDH and beta-2 microglobulin levels were significantly elevated in our patients, a finding similar to other published studies.[7, 14, 17, 18] M-band (monoclonal protein band) is detectable in 85.15% of our patients, which is in line with the findings of previous studies.[7, 12, 14, 19, 20] Immunofixation was utilized to detect and characterize the types of antibodies and clonal patterns. We observed that the most prevalent antibody type was IgG, present in 83.33% of our patients, which is higher than that observed by Kyle et al.,(52%) while lower than Sharma S et al., who found it in 90% of his patients.[13, 14] (Table 5) Additionally, we identified elevated levels of SFLC, with kappa being elevated in 87% of patients and lambda in 40.74% with the K/L ratio being higher in 74% of patients. Increased levels of SFLC were similarly documented by Kyle et al.[14] The present study found that 62.96% of patients had a hypercellular bone marrow with more than 50% of plasma cells in 40.7%, and suppression of erythroid and myeloid cells in 46.30%. This is comparable to findings in previous studies where the percentage of plasma cells exceeding 50% was reported as 46% by Kyle et al. and 27% by Sheikh et al.[14, 20]

Table 5. Comparison of laboratory parameters in patients with published studies.

Studies	Number of Patients	Anemia & Rouleaux Formation (RF) (%)	Thrombocytopenia (%)	Hypercalcemia (%)	Low Sr. Albumin (<3.5 gm/dl) (%)	Sr. LDH (above normal) (%)	Renal Function Dysfunction (%)	Serum Protein Electrophoresis (M-band) (%)	Bence-Jones Protein (Urine) (%)	Beta2 Microglobulin (>3.5) (%)	Immunoixation IgG type (%)
Kyle RA et al., 2003[14]	1027	73	5	28	15	-----	48	82	94	67	52
Kaur P et al., 2014[7]	28	92.7 RF 82.1	25	46.4	-----	78.5	86.4	92.8	-----	71.4	-----
Sultan S et al., 2016[15]	61	40.9	22.9	47.5	-----	-----	40.9	-----	-----	-----	-----
Pegu AK et al., 2016[12]	44	93	-----	23	59	-----	20	91	14	-----	-----
Shin J et al., 2017[17]	32	29	23	28	28	37	13	-----	-----	48	-----
Kaushik R et al., 2017[19]	51	45	23.5	11.76	-----	-----	15.6	83	-----	-----	-----
Jakhetia H et al., 2019[18]	30	77 RF 47	-----	37	47	40	30	-----	57	-----	-----
Sheik N et al., 2019[20]	26	70 RF 57	27	32	-----	-----	35	100	27	-----	-----
Sharma S et al., 2020[13]	37	90	-----	54	-----	-----	45.9	-----	16.2	-----	90
Mishra D et al., 2021[16]	49	80	12	20	-----	-----	39	-----	-----	-----	-----
Present study	54	74.07 RF 64.8	18.52	75.93	62.96	35.19	62.96	85.15	55.56	98.15	83.33

According to the Durie-Salmon staging system, most of our cases were classified as stage III (68.5%), which closely aligns with Kaur P et al. (64.3%) findings.[7] Stratifying our patients according to ISS staging found most of our patients in Stage II (59.25%) of the disease. The primary constraints in our study included the absence of cytogenetics/FISH testing, preventing the stratification of patients according to the RISS staging system.

5. Conclusion

Our study provides valuable insights into the demographic, clinical, and laboratory characteristics of MM patients in our region, emphasizing the importance of early detection and intervention. Multiple myeloma is a disease of middle-aged and elderly with multiple comorbidities. The clinical presentation can thus be variable and can come to the physician's attention with complaints of generalized weakness and pallor due to anemia rather than bone pains. The study also observed a notable incidence of hypercalcemia potentially linked to late-stage presentations at the tertiary care referral hospital. Our limited resource setting and inability to perform cytogenetics/FISH testing impacted our ability to stratify patients per the RISS system. Despite these limitations, this research contributes to the comprehensive knowledge of MM's clinical and laboratory aspects, facilitating better disease management. Further research and collaborative efforts with larger cohorts, longer follow-up durations, and implementation of the RISS system could offer deeper insights into this complex hematological malignancy.

Conflict of Interest

The authors declared that there is no conflict of interest.

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