RESEARCH PAPER

Clinical Profile of Newly Diagnosed Multiple Myeloma: A Single-Centre Descriptive Study

Akshay Mehta[1], Monica Bhagat[2], Amandeep Singh[3], Harmeet Pal Dhooria[4], Davinder Paul[5]

[1]Senior Resident, Department of Gastroenterology, Dayanand Medical College & Hospital, Ludhiana, India
[2]Assistant Professor, Department of Medicine, Dayanand Medical College & Hospital, Ludhiana, India
[3]Assistant Professor, Department of Pulmonary Medicine, Dayanand Medical College & Hospital, Ludhiana, India
[4]Professor, Department of Medicine, Dayanand Medical College & Hospital, Ludhiana, India
[5]Director and Head, Department of Medical Oncology, Fortis, Ludhiana, India

Abstract

Background

Multiple myeloma (MM) is a plasma cell malignancy characterized by heterogeneous clinical presentation and variable disease burden at diagnosis. Patterns of presentation may differ across healthcare settings, particularly where referral delays and resource constraints influence stage at detection. This study aimed to describe the baseline clinical and molecular characteristics of newly diagnosed MM patients at a tertiary care centre and evaluate their association with Revised International Staging System (R-ISS) stage.

Methods

This prospective observational study included 62 patients with newly diagnosed multiple myeloma evaluated over a one-year period at a tertiary care centre in North India. Diagnosis and staging were performed using the Revised International Myeloma Working Group criteria and the Revised International Staging System (R-ISS). Clinical features, laboratory parameters, imaging findings, bone marrow characteristics, and cytogenetic abnormalities detected by fluorescence in situ hybridization were analyzed. Associations between baseline variables and disease stage were assessed using chi-square and fisher's tests.

Results

The median age was 62 years (range: 35–75), and 36/62 (58.1%) patients were male. Stage II and stage III disease were observed in 28/62 (45.2%) and 34/62 (54.8%) patients, respectively; no patients presented with stage I disease. Severe anemia (24/62, 38.7%), hypoalbuminemia (35/62, 56.5%), elevated beta-2 microglobulin (49/62, 79%), and elevated LDH (42/62, 67.7%) were significantly associated with stage III disease ($p \leq 0.001$). Cytogenetic abnormalities were detected in 33/62 (53.3%), including high-risk abnormalities in 20/62 (32.3%).

Conclusion

In this single-centre cohort, most patients presented with R-ISS stage II–III disease and significant biochemical abnormalities. Hemoglobin, serum albumin, beta-2 microglobulin, and LDH were significantly associated with advanced stage. These routinely available parameters may support initial risk assessment at diagnosis, particularly in settings where access to comprehensive molecular testing is limited.

Keywords: multiple myeloma; Revised International Staging System; beta-2 microglobulin; lactate dehydrogenase; anemia;

How to cite this article: Mehta A, Bhagat M, Singh A, Dhooria HP, Paul D. Clinical Profile of Newly Diagnosed Multiple Myeloma: A Single-Centre Descriptive Study. Int J Drug Deliv Technol. 2026;16(6s): 497-506; DOI: 10.25258/ijddt.16.6s.74

Source of support: None

Conflict of interest: None

Introduction

Multiple myeloma (MM) is a malignant plasma cell disorder characterized by clonal expansion of plasma cells in the bone marrow, leading to monoclonal immunoglobulin production and associated end-organ damage. Although the incidence of MM is lower in Asian populations compared to Western countries, a steady rise in incidence has been observed in recent years, particularly in developing nations [1]. Lower reported incidence of multiple myeloma in Asian populations has been attributed to demographic structure, genetic susceptibility, environmental

exposures, and historically limited cancer registry coverage and diagnostic access, whereas the recent rise likely reflects population aging, improved case ascertainment, and wider availability of advanced diagnostics [1,2].

MM constitutes approximately 1% of all malignancies worldwide. According to 2021 data, India accounts for nearly 1.23% of all reported cancers. The median age at diagnosis typically ranges between 65 and 70 years, and only a small proportion of cases around 2% are identified in individuals younger than 40 years of age. [3]. Diagnosis is based on the presence of clonal bone marrow plasma cells or biopsy-proven plasmacytoma, along with myeloma-defining events such as hypercalcemia, renal insufficiency, anemia, or osteolytic bone lesions. The inclusion of biomarkers such as ≥60% clonal plasma cells, an abnormal free light chain ratio, or focal lesions on Magnetic Resonance Imaging (MRI) has refined early diagnosis and risk stratification [1].

Clinically, MM manifests with multi-organ involvement, including bone pain, pathological fractures, anemia, renal dysfunction, hypercalcemia, recurrent infections, and neurological complications. Bone disease results from increased osteoclastic activity with suppression of osteoblastic bone formation, leading to osteolytic lesions and fractures [4]. Bone pain and anemia remain the most frequent presenting complaints, while renal impairment and hypercalcemia contribute substantially to morbidity [5].

Clinical manifestations result from marrow infiltration by malignant plasma cells and monoclonal protein secretion. Anemia occurs in 40–73% of patients at diagnosis and contributes significantly to fatigue. Anemia in multiple myeloma is multifactorial and not solely due to marrow infiltration. Key mechanisms include renal dysfunction with reduced erythropoietin production and inflammation-mediated suppression of erythropoiesis [6,7]. Bone pain is reported in approximately 80% of cases, with lytic lesions, osteoporosis, or fractures seen in approximately three-quarters of patients on conventional imaging [6]. Renal dysfunction, present in about one-quarter of patients at diagnosis, may result from cast nephropathy, hypercalcemia, dehydration, or nephrotoxic exposures. Hyperviscosity and neurological complications may also occur, ranging from radiculopathy to spinal cord compression and, rarely, POEMS (Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal protein (or M-protein), and Skin changes) syndrome [1,8].

The incidence of MM is increasing in Asian countries, posing a growing challenge to healthcare systems with limited resources. In India, MM accounts for approximately 13% of hematological malignancies and is associated with significant morbidity due to complications such as renal failure, infections, anemia, osteolytic bone disease, and amyloidosis [7]. Despite being symptomatic at presentation in most cases, up to 10–15% of patients may initially remain asymptomatic, leading to delayed diagnosis and suboptimal referral pathways. The rising incidence of multiple myeloma in developing countries likely reflects both improved diagnosis and referral pathways, as well as demographic changes such as population aging, suggesting a combination of better detection and a true increase in cases [1,5].

There is a paucity of Indian data systematically evaluating clinical presentation and baseline investigations across different stages of newly diagnosed MM. This study was therefore undertaken to describe the clinical profile of newly diagnosed multiple myeloma patients in a tertiary care setting, with the aim of facilitating earlier recognition and improved diagnostic strategies.

Materials and Methods

Study Design and Setting

This prospective observational study was conducted in the Departments of Medicine, Oncology at Dayanand Medical College and Hospital (DMCH), Ludhiana, Punjab, India. The study was approved by the Institutional Ethics Committee of Dayanand Medical College and Hospital, Ludhiana. Written informed consent was obtained from all participants.

Study Population

All consecutive patients newly diagnosed with multiple myeloma (MM) during a one-year period from March 2021 to February 2022 were screened for inclusion. Both inpatients and outpatients were eligible for enrolment.

Sample Size

This study was designed as a descriptive observational study. A formal a priori sample size calculation was not performed. Instead, a convenience-based sampling approach was used, and all eligible patients newly diagnosed with multiple myeloma during the defined study period were included. The final sample size was therefore determined by the number of patients meeting inclusion criteria over the one-year enrolment period. The sample size of 62 represents all consecutive newly diagnosed patients during the one-year enrolment period. As a prospective descriptive study, the sample size was determined by case accrual rather

than formal power calculation. All patients who fulfilled the inclusion criteria and did not meet any exclusion criteria were enrolled. No additional eligible patients were excluded beyond the predefined exclusion criteria. Patients who declined consent were not enrolled.

Inclusion Criteria

Patients were included if they met the following criteria:

1. Newly diagnosed cases of multiple myeloma.
2. Willingness to participate and provision of written informed consent.

Exclusion Criteria

Patients were excluded if they had:

1. Previously diagnosed multiple myeloma on follow-up.
2. Monoclonal gammopathy of undetermined significance (MGUS).
3. Plasma cell leukemia.
4. Declined consent for participation.

Diagnostic Criteria

The diagnosis of multiple myeloma was made in accordance with the Revised International Myeloma Working Group (IMWG) criteria published in 2014. Multiple myeloma was diagnosed in patients with ≥10% clonal plasma cells in the bone marrow or a biopsy-confirmed bony or extramedullary plasmacytoma, together with at least one myeloma-defining event [9]. Plasma cell percentage was determined from bone marrow aspirate smears and/or trephine biopsy sections. When both were available, the higher percentage was considered for analysis. Clonality was assessed morphologically and supported by immunophenotypic findings where available.

In addition, specific biomarkers indicative of malignant plasma cell activity were considered diagnostic, namely ≥60% clonal plasma cells in the bone marrow, an involved-to-uninvolved serum free light chain ratio ≥100 with the involved light chain concentration ≥100 mg/L, or the presence of more than one focal lesion measuring ≥5 mm on magnetic resonance imaging. Smoldering multiple myeloma was defined according to IMWG criteria and was excluded from the study, as the analysis was restricted to newly diagnosed symptomatic multiple myeloma.

Data Collection

After obtaining informed consent, demographic details, clinical history, physical examination findings, and laboratory parameters were recorded using a predesigned proforma. Laboratory data and molecular workup were obtained from patient medical records. Baseline laboratory investigations included complete blood count, peripheral smear, erythrocyte sedimentation rate, renal and liver function tests, serum calcium (albumin-corrected), serum protein electrophoresis, immunofixation, and serum free light chain assay. Twenty-four–hour urine protein estimation and urine electrophoresis were performed when clinically indicated and were not uniformly available for all patients. Radiological evaluation was undertaken according to clinical indication and resource availability. Conventional skeletal survey was performed in the majority of patients, while advanced imaging modalities such as (Positron Emission Tomography and Computed Tomography) PET-CT or MRI were obtained selectively in cases with suspected occult lesions, neurological symptoms, or inconclusive radiographic findings. All patients underwent baseline radiological evaluation using conventional skeletal survey. PET-CT was performed selectively based on clinical indication and resource availability. Inflammatory markers, including C-reactive protein (CRP) and other acute-phase reactants, were not routinely measured at baseline and were therefore not included in the analysis.

All laboratory parameters were interpreted using reference ranges established by the central clinical laboratory of Dayanand Medical College and Hospital. Thresholds used for defining abnormalities were aligned with standard clinical practice and the Revised International Myeloma Working Group and Revised International Staging System criteria. All laboratory and clinical thresholds were predefined prior to statistical analysis based on established diagnostic criteria, institutional laboratory reference ranges, and R-ISS staging parameters. No post hoc threshold modifications were performed. Serum calcium values were recorded as albumin-corrected calcium and reported uniformly in mg/dL as per institutional laboratory reference standards. Renal function was assessed using serum creatinine values obtained at presentation. Estimated glomerular filtration rate (eGFR) using MDRD or CKD-EPI equations was not routinely calculated. Time from symptom onset to diagnosis or referral interval was not systematically recorded; therefore, diagnostic delay was not formally quantified in this study. For clarity and consistency, laboratory cut-offs applied in analyses are reported explicitly in the Results tables and were used uniformly across all sections of the manuscript.

Cytogenetic and Molecular Analysis

Interphase fluorescence in situ hybridization (FISH) analysis was performed on unenriched bone marrow samples. It was attempted in all enrolled patients at

baseline. Adequate analyzable results were obtained for all cases, and therefore no missing cytogenetic data were present for the study cohort. Plasma cells were identified morphologically on bone marrow smears, and hybridization signals were evaluated in these cells. CD138-based plasma cell enrichment was not performed. A total of 100 interphase nuclei were analyzed for each probe. FISH positivity was defined according to laboratory-standard cut-off values, with abnormalities considered positive when the proportion of nuclei showing the specific signal pattern exceeded 10% for deletion probes and 15% for translocation probes, in accordance with established diagnostic laboratory practices. This number is consistent with routine diagnostic cytogenetic laboratory practice and is considered adequate for the detection of clinically significant plasma cell–associated abnormalities in multiple myeloma, particularly in settings where plasma cell enrichment is not performed [9].

The probes used included:

- Zytolight SPEC (Specific Chromosome) Orange TP (tumour protein) p53/CEN (Centromere)17 SPEC Green dual-color probe for detection of deletion 17p (TP53).
- Zytolight SPEC FGFR3(Fibroblast Growth Factor Receptor)/IGH (Immunoglobulin Heavy Locus) dual-color dual-fusion probe for detection of t(4;14).
- Zytolight SPEC CCND1(Cyclin D1)/IGH dual-color dual-fusion probe for detection of t(11;14).
- Zytolight SPEC MAF(Musculoaponeurotic Fibrosarcoma)/IGH dual-color dual-fusion probe for detection of t(14;16).

Staging and Treatment

All patients were staged using the Revised International Staging System (R-ISS). R-ISS Stage III was defined as ISS stage III (beta-2 microglobulin ≥5.5 mg/L) in the presence of either high-risk cytogenetic abnormalities (t(4;14), t(14;16), or del(17p)) or elevated serum LDH above the institutional upper limit of normal. High-risk cytogenetic abnormalities were defined a priori according to the R-ISS criteria and included t(4;14), t(14;16), or deletion 17p (TP53) detected by FISH. Other abnormalities, including t(11;14), were classified as standard-risk cytogenetics for the purpose of analysis. This classification was applied consistently across all analysis. Patients who did not meet criteria for stage I or III were classified as stage II. Induction regimens were selected independent of transplant intent, which was assessed subsequently and not analyzed as an outcome in this study.

Outcome Assessment

Short-term in-hospital outcomes were recorded for descriptive purposes and were not predefined study endpoints. At discharge, 59 patients (95.2%) were discharged or took discharge against medical advice, while three patients (4.8%) died during hospitalization. All deaths occurred in patients with R-ISS stage III disease and elevated markers of tumor burden (hemoglobin <8 g/dL, beta-2 microglobulin >3.5 mg/L, and LDH >225 IU/L). Given the limited sample size and short follow-up duration, no inferential statistical comparisons of mortality were performed.

Statistical Analysis

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 21 (IBM Corp., Chicago, IL, USA). Continuous variables were summarized using mean ± standard deviation when normally distributed and median with interquartile range (IQR) when skewed. For clinically relevant parameters, categorical cutoffs were additionally reported to facilitate staging and risk stratification. Categorical variables were presented as frequencies and percentages. Inferential statistical analysis was limited to chi-square tests for assessment of associations between categorical variables. Associations between categorical variables and R-ISS stage were assessed using the chi-square test. A two-tailed p-value <0.05 was considered statistically significant. No additional inferential statistical tests were performed. For chi-square analyses, the chi-square statistic (χ^2) with degrees of freedom and corresponding p-values were reported. Categorical variables were compared using Pearson's chi-square test. When expected cell counts were <5 or when zero frequencies were present in contingency tables, Fisher's exact test was applied. A p-value <0.05 was considered statistically significant.

Results

Study Population

A total of 62 newly diagnosed multiple myeloma patients were included during the study period (March 2021–February 2022). Of these, 36 patients (58.1%) were males and 26 (41.9%) were females, with a male-to-female ratio of 1.4:1. The median age at diagnosis was 62 years (range: 35–75 years). Most patients belonged to the 56–65-year age group (50.0%), followed by 66–75 years (32.2%). Fatigue was the most common presenting complaint, reported by 48 patients (77.4%), followed by weight loss or loss of appetite. A detailed description is shown in Table 1.

Table 1: Presenting Complaints in Newly Diagnosed Multiple Myeloma

Presenting Complaint	Number of Patients	Percentage
Fatigue	48	77.4
Weight loss / Loss of appetite	33	53.2
Bone pain	32	51.6
Fever	26	41.9
Dyspnea	19	30.7
Decreased urine output	16	25.8
Fractures	6	9.7
Altered sensorium	2	3.2

Legend: Patients could report more than one presenting symptom.

Physical Examination Findings

Pallor was the most frequent clinical sign, present in 50 patients (80.6%). Pedal edema was observed in five patients (8.1%). No patient had icterus, hepatosplenomegaly, or focal motor or sensory neurological deficits at presentation.

Hematological and biochemical parameters

Hemoglobin levels were <8 g/dL in 24 patients (38.7%), between 8–10 g/dL in 22 patients (35.5%), and >10 g/dL in only 16 patients (25.8%). So, anemia was present in 46 out of 62 patients (74.2%). Thrombocytopenia (platelet count <1.5 x 10^9/L) was present in 16 patients (25.8%). Total leukocyte count was within the normal range (4–11 × 10^3/mm³) in 71% of patients. Erythrocyte Sedimentation Rate (ESR) was elevated (>50 mm/hour) in 55 patients (88.7%), of whom 11 patients (17.7% of the total cohort) had ESR values >100 mm/hour. Rouleaux formation was observed on peripheral blood smear in 61.3% of patients.

Serum creatinine levels >2 mg/dL were observed in 41 patients (66.1%). Hypercalcemia, defined as corrected serum calcium >11 mg/dL based on institutional laboratory reference ranges, was present in 53 patients (85.5%). Serum calcium values were uniformly interpreted as albumin-corrected calcium as reported by the institutional clinical laboratory. Hypoalbuminemia (serum albumin <3.5 g/dL) was noted in 35 patients (56.5%), and A/G ratio reversal (<1.1) was seen in 51 patients (82.3%). Elevated beta-2 microglobulin (>3.5 mg/L) was present in 49 patients (79%) with a mean level of 7.2 ± 5.3 mg/L. Serum LDH >225 IU/L were observed in 42 patients (67.7%). This is shown in Table 2.

Table 2: Hematological and Biochemical Parameters at Presentation (Using Institutional Laboratory Reference Ranges)

Parameter	Threshold / Category	Frequency (n=62)	Percentage
Hemoglobin	< 8 g/dL	24	38.7
	8 – 10 g/dL	22	35.5
	> 10 g/dL	16	25.8
Platelet Count	Thrombocytopenia (<1.5 x 10^9/L)	16	25.8
ESR	> 50 mm/hour	55	88.7
	> 100 mm/hour	11	17.7
Renal Function	Serum Creatinine > 2 mg/dL (177µmol/L)	41	66.1
Calcium	Hypercalcemia >11 mg/dL (2.75 mmol/L)	53	85.5
Albumin	Hypoalbuminemia (<3.5 g/dL)	35	56.5
Tumor Burden	Elevated LDH (>225 IU/L)	42	67.7
	Elevated beta-2 Microglobulin (>3.5 mg/L)	49	79

Continuous laboratory parameters are additionally summarized using categorical thresholds to reflect clinically relevant cutoffs used in diagnostic criteria and staging systems. All biochemical parameters are reported using institutional laboratory reference units.

Legend: ESR = erythrocyte sedimentation rate; LDH = lactate dehydrogenase.

Radiological and Bone Marrow Findings

Radiological evaluation was performed in all 62 patients using conventional skeletal survey at baseline. PET-CT was available for a subset of patients based on clinical indication and institutional resource

availability. Skeletal survey and/or PET-CT demonstrated osteolytic lesions in 37 patients (59.7%). Diffuse osteopenia was seen in 11.3%, while fractures and vertebral collapses were observed in 12.9% of patients. Seven patients (11.3%) had normal skeletal imaging. Bone marrow examination demonstrated clonal plasma cell infiltration ≥10% on aspirate smear and/or trephine biopsy in 58 patients (93.5%), one patient (1.6%) had 10–30% clonal plasma cells on bone marrow examination and normal marrow in three patients (4.8%). In patients with bone marrow plasma cells <10%, the diagnosis of multiple myeloma was established based on biopsy-proven plasmacytoma in the presence of myeloma-defining events, in accordance with IMWG criteria. Plasma cell infiltration ≥30% was observed in 38.7% of patients. A detailed description is shown in Figure 1.

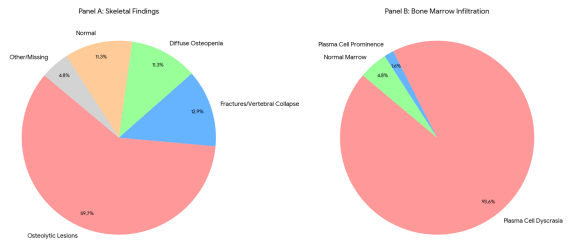

Figure 1. Bone marrow findings showing plasma cell dyscrasia with varying degrees of plasma cell infiltration.

Although renal impairment (serum creatinine >2 mg/dL) was observed in 41 patients (66.1%), detailed etiological classification of renal dysfunction (e.g., myeloma cast nephropathy, light-chain deposition disease, or chronic kidney disease unrelated to MM) was not systematically performed. Quantitative 24-hour Bence-Jones protein estimation was not uniformly available.

Staging and Treatment

According to the R-ISS, no patient presented with stage I disease. Stage II disease was observed in 28 patients (45.2%), while stage III disease was present in 34 patients (54.8%). Most patients (90.3%) required inpatient treatment. The most commonly used induction regimen was bortezomib, lenalidomide, and dexamethasone (41.9%), followed by bortezomib, cyclophosphamide, and dexamethasone (22.6%).

Induction therapy was administered according to institutional protocol and patient eligibility. Bortezomib was administered subcutaneously at a dose of 1.3 mg/m² on Days 1, 4, 8, and 11 of a 21-day cycle. Dexamethasone was administered at a dose of 20–40 mg weekly orally, adjusted according to age and tolerance. Lenalidomide, when used, was given at 25 mg orally on Days 1–21 of a 28-day cycle, with dose adjustments based on renal function. Cyclophosphamide, when included, was administered at 300 mg/m² weekly, oral or intravenous as per protocol. Dose modifications were made in elderly patients and those with renal impairment in accordance with standard practice guidelines. The details are shown in Figure 2.

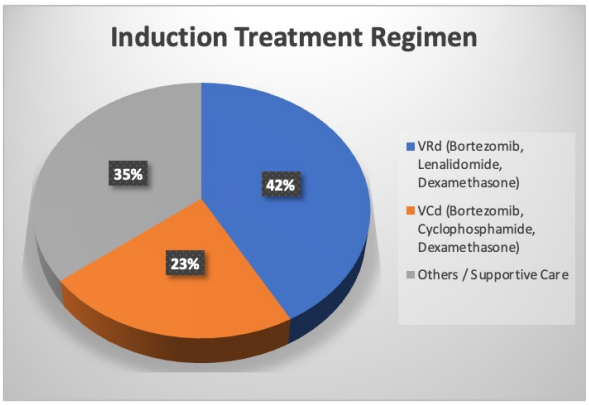

Figure 2: Induction chemotherapy regimens used in newly diagnosed multiple myeloma patients.

Outcome

At the time of assessment, 59 patients (95.2%) were discharged or took discharge against medical advice, while three patients (4.8%) died during hospitalization. The three deaths occurred in patients with hemoglobin <8 g/dL, elevated LDH, beta-2 microglobulin >3.5 mg/L, and R-ISS stage III disease. Molecular abnormalities detected by FISH were present in 33 patients (53.3%), while 29 patients (46.7%) had no detectable cytogenetic abnormalities. Standard-risk cytogenetics, predominantly t(11;14), were observed in 13 patients (21%), while the high-risk cytogenetic abnormalities, as defined by R-ISS criteria, were identified in 20 patients (32.3%) and included t(4;14) (n=10, 16.1%), t(14;16) (n=7, 11.3%), and deletion 17p (n=3, 4.9%).

Molecular Profile and Clinical Correlates

Patients with high-risk cytogenetic abnormalities showed numerically higher frequencies of anemia, renal impairment, hypercalcemia, hypoalbuminemia, elevated LDH, and elevated beta-2 microglobulin; however, these differences were not statistically significant (all $p > 0.05$). Deletion 17p was more frequently observed in patients with lower hemoglobin, elevated beta-2 microglobulin, elevated LDH, and R-ISS stage III disease; however, these differences did not reach statistical significance (all $p > 0.05$). However, no statistically significant differences were observed between molecular profile–positive and –negative groups with respect to age, sex, platelet count,

leukocyte count, serum calcium, renal function, or bone marrow plasma cell burden. Plasma cell burden was calculated using the higher value obtained from aspirate or biopsy when both were available.

Molecular Profile and Staging

High-risk cytogenetic abnormalities were distributed across both stage II and stage III disease. Deletion 17p and t(4;14) were observed more frequently among patients with R-ISS stage III disease. The association between specific cytogenetic abnormalities and R-ISS stage did not reach statistical significance. The degree of association is shown in Table 3.

Table 3: Association of Clinical and Laboratory Parameters With R-ISS Stage

Parameter	Stage II (n=28)	Stage III (n=34)	Test used	p-value
Male sex (%)	57.1	58.8	Chi-square	0.894
Hemoglobin <8 g/dL (%)	0	70.6	Fisher's exact	0.001
Serum albumin <3.5 g/dL (%)	17.9	88.2	Chi-square	<0.001
Beta-2 microglobulin >3.5 mg/L (%)	53.6	100	Fisher's exact	<0.001
LDH >225 IU/L (%)	28.6	100	Fisher's exact	<0.001

dL- decilitre

mg- milligram

LDH- Lactate Dehydrogenase

R-ISS- Revised Multiple Myeloma International Staging System

Categorical variables were compared using Pearson's chi-square test. Fisher's exact test was applied when expected cell counts were <5 or when zero frequencies were present.

Discussion

The demographic characteristics of the study population are consistent with contemporary epidemiological trends in multiple myeloma. Although the age distribution and male predominance observed in this cohort appear comparable to larger published series, the limited sample size precludes firm epidemiological conclusions [1,4]. The absence of any association between age or sex and disease stage in the present study suggests that demographic factors alone do not influence disease severity at diagnosis, a finding also supported by recent population-based analyses [2].

Fatigue was the most common presenting symptom, followed by weight loss, bone pain, and fever. Fatigue was frequently reported and may be multifactorial, potentially related to anemia, systemic inflammation, renal dysfunction, or other comorbid conditions rather than exclusively to marrow infiltration. Recent studies emphasize that fatigue and constitutional symptoms frequently precede classical CRAB (hypercalcemia, Renal insufficiency, Anemia and Bone lesions) manifestations and may contribute to delays in diagnosis, particularly in resource-limited settings [10,11]. The relatively high frequency of fractures and renal symptoms in this cohort is consistent with a high proportion of advanced disease at presentation, consistent with the high proportion of patients classified as R-ISS stage II and III.

Anemia was present in almost three-fourths of the cohort, with more than one-third of patients presenting with severe anemia. This finding is comparable to recent real-world data showing anemia in 70–90% of newly diagnosed patients [4]. Anemia in multiple myeloma is multifactorial and not solely dependent on marrow plasma cell burden. Contributing mechanisms include impaired erythropoietin production due to renal dysfunction, inflammatory cytokine–mediated suppression of erythropoiesis, iron dysregulation, nutritional deficiencies, and, less commonly, hemolysis. Therefore, the prevalence of anemia in this study should not be interpreted as entirely attributable to myeloma infiltration alone [5,7]. In the present study, a detailed etiological workup to distinguish these mechanisms was not systematically performed. Therefore, although anemia correlated with advanced stage, its precise attribution to myeloma-related marrow involvement cannot be conclusively established in all patients.

Renal impairment and hypercalcemia were observed in a majority of patients, reflecting classical end-organ damage. Recent studies have shown that renal dysfunction at diagnosis continues to be common despite advances in early detection, particularly in low- and middle-income countries [12]. The proportion of patients with renal dysfunction (66.1%) and hypercalcemia (85.5%) in our study was higher than what is usually reported in newly diagnosed multiple myeloma. This may be because our hospital is a tertiary referral center, where patients with more severe disease are more likely to be admitted. In addition, delays in diagnosis and referral may lead to patients presenting at a more advanced stage. Differences in how renal

function and calcium levels were measured may also have contributed to the higher observed rates. Therefore, these findings likely reflect referral patterns and late presentation rather than true biological differences in the disease.

Hypoalbuminemia and reversal of the albumin-globulin ratio were common findings. Serum albumin remains a well-validated surrogate of disease burden and inflammatory activity and continues to be an integral component of prognostic staging systems [9]. Elevated beta-2 microglobulin (>3.5 mg/L) and LDH (>225 IU/L) were observed in 79% and 67.7% of patients, respectively, consistent with advanced-stage disease at presentation. The higher frequency of elevated LDH compared to some published series may reflect referral bias toward more advanced cases or delayed presentation. Contemporary studies consistently identify these markers as key indicators of tumor mass, biological aggressiveness, and inferior survival outcomes [8,13]. Elevated beta-2 microglobulin and LDH were observed in 34/34 (100%) patients with stage III disease in this cohort; however, given the limited sample size, this finding should be interpreted cautiously.

Osteolytic lesions were the predominant radiological finding, consistent with the known pathophysiology of myeloma bone disease driven by increased osteoclastic activity and impaired osteoblast function. Recent imaging-based studies confirm that conventional skeletal surveys may underestimate early bone disease, although they remain widely used in resource-constrained settings [14]. The significant association between elevated alkaline phosphatase levels and fractures suggests that alkaline phosphatase may serve as a surrogate marker of skeletal damage in advanced disease. While alkaline phosphatase is not a routine prognostic marker in multiple myeloma, emerging evidence suggests its potential role in reflecting fracture risk and bone remodelling activity [3].

Bone marrow examination confirmed plasma cell dyscrasia in the vast majority of patients, with a substantial proportion demonstrating plasma cell infiltration ≥30%. High marrow plasma cell burden has been associated with aggressive disease biology and poorer outcomes in recent studies [15]. Notably, no patient in this cohort presented with R-ISS stage I disease. The high proportion of advanced-stage disease at presentation may reflect delayed recognition and referral, as reported in prior studies; however, diagnostic delay was not directly measured in the present cohort. Similar patterns have been reported in recent Indian studies, where early-stage myeloma remains underrepresented [16]. Most patients required inpatient management and were treated with proteasome inhibitor–based triplet regimens. During the study period (2021–2022), bortezomib-based triplets represented the standard induction approach at our institution. The limited use of anti-CD38–containing quadruplet regimens reflects real-world resource constraints and drug availability in our setting rather than contemporary global practice standards [4].

Molecular abnormalities were detected in over half of the cohort. t(11;14), classified as a standard-risk cytogenetic abnormality under the R-ISS, was the most frequently observed alteration, while high-risk abnormalities were present in a smaller subset of patients. Although classified as standard-risk in R-ISS, t(11;14) represents a biologically distinct subtype with heterogeneous clinical behavior and emerging therapeutic implications. [17]. High-risk cytogenetic abnormalities, including t(4;14), t(14;16), and deletion 17p, were present in a smaller subset but were associated with more severe biochemical derangements and adverse clinical features. Recent literature consistently demonstrates that deletion 17p confers particularly poor prognosis due to loss of TP53-mediated tumor suppression [18].

Despite these trends, no statistically significant association was observed between molecular profile and R-ISS stage in this cohort. This likely reflects limited sample size and underscores the complexity of myeloma biology, where cytogenetic risk and clinical stage do not always align [19]. In-hospital mortality was low; however, deaths occurred exclusively in patients with advanced disease, severe anemia, elevated LDH, and high beta-2 microglobulin levels. These findings are consistent with recent outcome studies demonstrating that biochemical markers of tumor burden and aggressive disease biology remain strong predictors of early mortality [20].

Limitations

This study has several limitations. First, it was conducted at a single tertiary care center with a relatively small sample size, which may limit the generalizability of the findings. Second, long-term outcomes such as progression-free survival and overall survival were not assessed due to the short follow-up period. Third, advanced imaging modalities and comprehensive genomic profiling were not uniformly available, potentially leading to underestimation of early skeletal disease and molecular risk. Fourth, owing to the relatively small sample size, several subgroup analyses, particularly those involving cytogenetic subgroups and stage-wise comparisons,

may have been underpowered to detect statistically significant associations. Therefore, the absence of statistically significant differences in certain analyses should be interpreted with caution and may not reflect true lack of association.

Fifth, treatment response and transplant outcomes were not systematically analyzed, limiting prognostic interpretation beyond baseline characteristics. In addition to this the absence of testing for 1q21 gain/amplification and t(14;20) may have led to underestimation of high-risk cytogenetic disease. Consequently, a subset of patients classified as standard-risk may have harboured additional adverse genomic features not captured by the limited FISH panel. This limitation reflects real-world diagnostic constraints in resource-limited settings. Lastly, we had limitations such as the absence of systematic analysis of heavy/light chain isotypes, κ/λ ratio distribution, and Bence–Jones proteinuria. The causality of anemia and renal impairment was not formally investigated, and specific aetiologies such as cast nephropathy or deposition disease were not uniformly characterized. Conventional cytogenetics was not performed, and the FISH panel did not include t(14;20) or 1q21 amplification, potentially leading to underestimation of high-risk disease. These factors limit comprehensive biological characterization of the cohort

Future Directions

Future studies should focus on multicentre, larger-scale cohorts to better characterize regional variations in disease presentation and molecular risk profiles. Incorporation of longitudinal follow-up data would help elucidate the impact of baseline clinical and molecular features on survival outcomes. Expanded access to advanced imaging and next-generation sequencing may further refine risk stratification. Additionally, strategies aimed at earlier diagnosis, including physician awareness and streamlined referral pathways, are needed to reduce the burden of advanced-stage disease at presentation in resource-constrained settings.

Conclusion

This prospective study highlights that the majority of newly diagnosed multiple myeloma patients in a tertiary care Indian setting present with advanced disease and significant end-organ damage. Severe anemia, hypoalbuminemia, elevated beta-2 microglobulin, and elevated LDH levels were significantly associated with advanced R-ISS stage ($p \leq 0.001$ for all comparisons). High-risk cytogenetic abnormalities demonstrated descriptive trends toward adverse clinical features; however, no statistically significant associations were identified. Therefore, their distribution across stages reflects the biological heterogeneity of multiple myeloma. Early recognition and systematic evaluation using readily available clinical and biochemical parameters may facilitate timely diagnosis and potentially improve outcomes.

References

1. Malard F, Neri P, Bahlis NJ, et al. Multiple myeloma. Nat Rev Dis Primers. 2024;10:45. 10.1038/s41572-024-00529-7
2. Cook JM. Racial disparities in multiple myeloma and access to stem cell transplantation. Blood Cancer J. 2024;14(1):120. 10.1038/s41408-024-01097-5.
3. Pydi VR, Bala SC, Kuruva SP, Chennamaneni R, Konatam ML, Gundeti S. Multiple Myeloma in Young Adults: A Single Centre Real World Experience. Indian J Hematol Blood Transfus. 2021;37(4):679-83. 10.1007/s12288-021-01410-3.
4. Terpos E, Ntanasis-Stathopoulos I, Gavriatopoulou M, Dimopoulos MA. Pathogenesis of bone disease in multiple myeloma: from bench to bedside. Blood cancer J. 2018;8(1):7. 10.1038/s41408-017-0037-2
5. Rajkumar SV. Multiple myeloma: 2022 update on diagnosis, risk stratification, and management. Am J Hematol. 2022;97(8):1086-107. 10.1002/ajh.26590.
6. Kristinsson SY, Anderson WF, Landgren O. Improved long-term survival in multiple myeloma up to the age of 80 years. Leukemia. 2014;28(6):1346-8. 10.1038/leu.2014.23
7. Liu L, Yu Z, Cheng H, et al. Multiple myeloma hinders erythropoiesis and causes anaemia owing to high levels of CCL3 in the bone marrow microenvironment. Sci Rep. 2020;10(1):20508. 10.1038/s41598-020-77450-y
8. Dong M, Zhang J, Han X, et al. Baseline peripheral neuropathy is associated with age and prognosis in newly diagnosed multiple myeloma patients. Sci Rep. 2022;12:10061. 10.1038/s41598-022-13935-2
9. Palumbo A, Avet-Loiseau H, Oliva S, et al. Revised international staging system for multiple myeloma: a report from International Myeloma Working Group. J Clin Oncol. 2015;33(26):2863-

9. 10.1200/JCO.2015.61.226

10. Scheid C, Landgren O. Early detection of multiple myeloma: A first step towards a screening programme. Br J Haematol. 2024;204(2):393-4. 10.1111/bjh.19274.
11. Garfall AL. New biological therapies for multiple myeloma. Annu Rev Med. 2024;75(1):13-29. 10.1146/annurev-med-050522-033815
12. Zhang Y, Pan J, Kang H, Peng S, Tung TH, Shen B. Prognosis of concurrent renal impairment at diagnosis of multiple myeloma: a systematic review. Ann Med. 2024;56(1):2380301. 10.1080/07853890.2024.2380301.
13. Espinoza-Zamora R, Zapata-Canto NP, Aguilera-Urbina LD, Cruz-Velazquez J, Reyes-Maldonado E, Vela-Ojeda J. Increased LDH Remains a Crucial Prognostic Factor in Patients With Multiple Myeloma. Arch Med Res. 2025;56(6):103239. 10.1016/j.arcmed.2025.103239
14. Hillengass J, Usmani S, Rajkumar SV, et al. International Myeloma Working Group consensus recommendations on imaging in monoclonal plasma cell disorders. Lancet Oncol. 2019;20(6):e302–e12. 10.1016/S1470-2045(19)30309-2
15. Rees MJ, Kumar S. High-risk multiple myeloma: redefining genetic, clinical, and functional high-risk disease in the era of molecular medicine and immunotherapy. Am J Hematol. 2024;99(8):1560-75. 10.1002/ajh.27327
16. Biswal P, Pandey RD, Singh G. Clinicopathological profile of multiple myeloma at a tertiary care hospital in a resource-poor setting: a retrospective study. J Hematol Allied Sci. 2023;3:103–8. 10.25259/JHAS_48_2023
17. Lakshman A, Alhaj Moustafa M, Rajkumar SV, et al. Natural history of t (11; 14) multiple myeloma. Leukemia. 2018;32(1):131-8. 10.1038/leu.2017.204
18. Walker BA, Mavrommatis K, Wardell CP, et.al. A high-risk, Double-Hit, group of newly diagnosed myeloma identified by genomic analysis. Leukemia. 2019;33(1):159-70. 10.1038/s41375-018-0196-8
19. Rasche L, Kortüm KM, Raab MS, Weinhold N. The impact of tumor heterogeneity on diagnostics and novel therapeutic strategies in multiple myeloma. Int J Mol Sci. 2019;20(5):1248. 10.3390/ijms20051248
20. Costa LJ, Gonsalves WI, Kumar SK. Early mortality in multiple myeloma. Leukemia. 2015;29(7):1616-8. 10.1038/leu.2015.33