Bone Marrow Findings And Prognostic Indicators In Multiple Myeloma Patients

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KEYWORDS

Multiple Myeloma, Bone Marrow, Immunophenotyping, Cytogenetics, R-ISS.

ABSTRACT:

Background: Multiple myeloma (MM) is a plasma cell malignancy with heterogeneous clinical and pathological features. Early characterization of bone marrow findings, immunophenotypic profiles, and cytogenetic abnormalities is essential for risk stratification and guiding treatment strategies, especially in resource-limited settings like Bangladesh. **Methods:** This cross-sectional observational study was conducted in the Department of Haematology at Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, from July 2022 to June 2023. A total of 60 newly diagnosed, untreated MM patients were included based on clinical features, biochemical parameters, serum protein electrophoresis, and bone marrow examination. **Results:** The mean age of patients was 59.8 ± 9.6 years, with 61.7% being male and 58.3% from rural areas. Common presenting symptoms included bone pain (76.7%), anemia (70.0%), and fatigue (65.0%). Laboratory results showed anemia (mean Hb: 8.9 ± 1.6 g/dL), elevated ESR, calcium, creatinine, β2-microglobulin, LDH, and CRP. Bone marrow plasma cell infiltration ranged from 31–60% in 46.7% and >60% in 30.0% of patients. The most frequent infiltration pattern was diffuse (40.0%), and 45.0% had mature plasma cell morphology. Immunophenotyping showed universal CD138 positivity, with high expression of CD38 (98%) and aberrant CD56 (84%). CD19 negativity was seen in 90% of cases. Cytogenetic abnormalities included gain of 1q21 (20.0%), del(17p13) (18.0%), and t(4;14) (14.0%). Based on R-ISS, 48.3% were Stage II, 31.7% Stage III, and 20.0% Stage I. **Conclusion:** A significant proportion of MM patients presented with advanced disease, highlighting the need for early diagnosis and comprehensive diagnostic workup for better risk stratification and management.

INTRODUCTION

Multiple myeloma (MM) is a malignant plasma cell disorder characterized by clonal proliferation of plasma cells in the bone marrow, leading to a spectrum of clinical manifestations such as anemia, hypercalcemia, renal impairment, lytic bone lesions, and increased susceptibility to infections [1]. Globally, MM accounts for approximately 1% of all malignancies and 10–15% of hematological cancers [2]. In Bangladesh, the burden of MM has been gradually increasing, likely due to improved diagnostic capabilities and increased awareness, although exact epidemiological data remain limited [3].

The diagnosis of multiple myeloma relies on a combination of clinical, laboratory, radiologic, and bone marrow findings [4]. Bone marrow examination plays a pivotal role in confirming the diagnosis, revealing the extent and pattern of plasma cell infiltration, as well as identifying morphologic variants that may have prognostic relevance [5]. In addition to morphological evaluation, immunophenotyping using flow cytometry has become a valuable diagnostic tool, aiding in the distinction of malignant from reactive plasma cells based on aberrant antigen

expression [6]. Cytogenetic abnormalities, such as del(17p), t(4;14), and gain of 1q21, are recognized as critical prognostic markers and are now incorporated into the Revised International Staging System (R-ISS) for risk stratification [7].

Despite the evolution in understanding MM pathobiology, limited studies have explored the detailed bone marrow findings and cytogenetic profiles of patients in the Bangladeshi population [8]. Moreover, the availability of advanced diagnostic tools such as flow cytometry and FISH is often restricted to tertiary care centers and is subject to financial constraints, posing challenges to comprehensive risk assessment. In resource-constrained settings like Bangladesh, a thorough evaluation of bone marrow morphology and basic laboratory markers remains indispensable in guiding initial diagnosis and prognosis [9].

Several bone marrow characteristics—such as the degree of plasma cell infiltration, infiltration pattern, and the presence of atypical or plasmablastic morphology—have been associated with adverse outcomes [10]. Additionally, immunophenotypic markers like CD56 expression and cytogenetic abnormalities have been correlated with disease aggressiveness and treatment response [11]. Understanding the local patterns of these parameters is essential for optimizing disease management and stratifying patients for risk-adapted therapy [12].

In this context, we conducted a study to evaluate the bone marrow morphology, immunophenotypic profile, and cytogenetic findings in patients newly diagnosed with multiple myeloma at a tertiary care center in Bangladesh. Our aim was to identify key prognostic indicators that may help in early risk stratification and support clinical decision-making in low-resource settings. By characterizing these diagnostic features in our patient population, this study seeks to contribute to the growing body of knowledge on MM in South Asia and underscore the importance of integrating morphological and molecular data for better prognostic assessment.

METHODOLOGY & MATERIALS

This cross-sectional observational study was conducted in the Department of Haematology at Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, from July 2022 to June 2023. A total of 60 patients diagnosed with multiple myeloma were enrolled based on clinical presentation, biochemical profile, serum protein electrophoresis, and bone marrow examination findings. Inclusion criteria included newly diagnosed and untreated multiple myeloma patients aged over 18 years who provided informed consent. Patients were excluded if they had received prior chemotherapy, had other concomitant hematological malignancies, or if their clinical and laboratory data were incomplete. Detailed clinical history, physical examination, and relevant biochemical parameters including serum calcium, creatinine, albumin, β2-microglobulin, LDH, and CRP were documented at baseline. Bone marrow aspiration and trephine biopsy were performed in all patients, and the extent of plasma cell infiltration, infiltration pattern (interstitial, nodular, or diffuse), and morphological variants (mature, atypical, or plasmablastic) were recorded. Immunophenotyping by flow cytometry was performed to assess expression of CD138, CD38, CD56, CD19, and CD45 in 50 patients due to test availability and affordability. Similarly, fluorescence in situ hybridization (FISH) was conducted in those same 50 patients to identify high-risk cytogenetic abnormalities, including del(17p13), t(4;14), and gain of 1q21. Light chain restriction (kappa or lambda) was also determined. Risk stratification was done according to the Revised International Staging System (R-ISS), incorporating serum albumin, β2-microglobulin, LDH levels, and cytogenetic findings. Data were entered and analyzed using IBM SPSS version 22.0. Descriptive statistics were used to summarize categorical variables as frequencies and percentages, while continuous variables were expressed as means with standard deviations.

RESULTS

Table 1: Baseline Demographic and Clinical Characteristics (n = 60)

Variable	Frequency (n)	Percentage (%)
Gender		
- Male	37	61.70%
- Female	23	38.30%
Age (years)	59.8 ± 9.6	
Rsidence		
- Rural	35	58.30%
- Urban	25	41.70%
Presenting Symptoms		
- Bone pain	46	76.70%
- Fatigue/Weakness	39	65.00%
- Recurrent infections	18	30.00%
- Renal impairment	15	25.00%
- Anemia (clinical)	42	70.00%

Table 1 presents the baseline demographic and clinical characteristics of the 60 patients diagnosed with multiple myeloma. The majority were male (61.7%) with a mean age of 59.8 ± 9.6 years. Most patients resided in rural areas (58.3%). Common presenting symptoms included bone pain (76.7%), clinical anemia (70.0%), fatigue or weakness (65.0%), recurrent infections (30.0%), and renal impairment (25.0%).

Table 2: Laboratory and Biochemical Parameters at Diagnosis

Parameter	Mean ± SD
Hemoglobin (g/dL)	8.9 ± 1.6
Total WBC (×10⁹/L)	6.5 ± 2.4
Platelet Count (×10⁹/L)	182.4 ± 52.7
ESR (mm/hr)	96.1 ± 25.3
Serum Calcium (mg/dL)	10.8 ± 1.4
Serum Creatinine (mg/dL)	2.1 ± 1.3
Serum Albumin (g/dL)	3.2 ± 0.6
β2-microglobulin (mg/L)	5.9 ± 2.3
LDH (U/L)	312 ± 85
CRP (mg/L)	21.4 ± 10.2

Table 2 summarizes the laboratory and biochemical parameters of the study population at diagnosis. Patients had a mean hemoglobin level of 8.9 ± 1.6 g/dL and elevated ESR (96.1 ± 25.3 mm/hr), reflecting anemia and systemic inflammation. Mean serum calcium was 10.8 ± 1.4 mg/dL, and creatinine was 2.1 ± 1.3 mg/dL, indicating frequent renal involvement. Other key parameters included β2-microglobulin (5.9 ± 2.3 mg/L), LDH (312 ± 85 U/L), CRP (21.4 ± 10.2 mg/L), and serum albumin (3.2 ± 0.6 g/dL), which contributed to risk stratification and prognostic assessment.

Table 3: Bone Marrow Morphology and Infiltration Patterns (n = 60)

Variable	Frequency (n)	Percentage (%)
Plasma Cell Infiltration		
- 10–30%	14	23.30%
- 31–60%	28	46.70%
- >60%	18	30.00%
Infiltration Pattern		
- Interstitial	22	36.70%
- Diffuse	24	40.00%
- Nodular/Focal	14	23.30%
Plasma Cell Morphology		
- Mature	27	45.00%
- Atypical	21	35.00%
- Plasmablastic	12	20.00%

Table 3 illustrates the bone marrow morphological findings and infiltration patterns among the 60 multiple myeloma patients. Plasma cell infiltration ranged from 10–30% in 23.3% of patients to over 60% in 30.0%. Diffuse infiltration was the most common pattern (40.0%), followed by interstitial (36.7%) and nodular/focal (23.3%). Regarding plasma cell morphology, mature plasma cells were observed in 45.0% of cases, while atypical and plasmablastic features were noted in 35.0% and 20.0% of patients, respectively, indicating variable disease aggressiveness.

Table 4: Immunophenotyping and Cytogenetic Findings (n = 50)

Marker / Finding	Frequency (n)	Percentage (%)
$CD138^+$	50	100.00%
$CD38^+$	49	98.00%
$CD56^+$ (aberrant)	42	84.00%
$CD19^-$	45	90.00%
CD45 variable	28	56.00%
Light Chain Restriction		
- Kappa	31	62.00%
- Lambda	19	38.00%
Cytogenetic Abnormalities		

- del(17p13)	9	18.00%
- t(4;14)	7	14.00%
- Gain of 1q21	10	20.00%
- Normal cytogenetics	24	48.00%

Table 4 shows the immunophenotypic and cytogenetic findings in 50 patients for whom advanced testing was available. All patients expressed CD138, and most were $CD38^+$ (98.0%) and $CD19^-$ (90.0%), consistent with malignant plasma cell immunophenotype. Aberrant CD56 expression was observed in 84.0% of cases, while CD45 expression was variable in 56.0%. Light chain restriction analysis revealed kappa dominance in 62.0% and lambda in 38.0%. Among cytogenetic abnormalities, gain of 1q21 (20.0%), del(17p13) (18.0%), and t(4;14) (14.0%) were identified, with 48.0% showing normal cytogenetics.

Table 5: Risk Stratification Based on Revised ISS (n = 60)

R-ISS Stage	Frequency (n)	Percentage (%)
Stage I	12	20.00%
Stage II	29	48.30%
Stage III	19	31.70%

Table 5 presents the risk stratification of patients according to the Revised International Staging System (R-ISS). Among the 60 patients, 48.3% were classified as Stage II, while 31.7% fell into the high-risk Stage III category. Only 20.0% were categorized as Stage I, indicating that the majority presented with intermediate to high-risk disease at diagnosis.

DISCUSSION

This study provides an in-depth overview of clinical, laboratory, morphological, immunophenotypic, and cytogenetic features in newly diagnosed multiple myeloma (MM) patients from a tertiary care center in Bangladesh. The findings are largely consistent with regional and international literature, with some variations possibly reflecting local demographic, environmental, and healthcare factors.

The mean age of our cohort (59.8 years) is consistent with regional studies, such as that by Sharmin *et al*., who reported a mean age of 58.6 years in newly diagnosed MM patients in Dhaka [13]. Male predominance (61.7%) was also observed, which aligns with the findings of Sultan *et al*. and Madu *et al*., suggesting a global trend of higher MM incidence among males [14, 15].

Bone pain, anemia, and fatigue were the predominant clinical presentations, corroborating earlier findings by Basit *et al*. and Firth, who emphasized skeletal-related events and cytopenias as hallmark features of MM [16, 17]. The presence of hypercalcemia, elevated creatinine, and increased β2-microglobulin in a significant portion of our cohort is consistent with advanced disease at diagnosis, reflecting the delayed presentation typical in low-resource settings [15].

Bone marrow morphology showed moderate to marked plasma cell infiltration in most patients, with a predominance of diffuse and interstitial patterns. These histological patterns have been linked with aggressive disease and worse prognosis [18, 19]. The presence of atypical and plasmablastic morphology in 55% of cases (combined) further underlines the disease severity, as supported by studies showing these morphologies to be associated with higher proliferative indices and poorer outcomes [20, 21].

Immunophenotyping revealed a high rate of CD138 and CD38 positivity, confirming plasma cell lineage, while aberrant CD56 expression (84%) and CD19 negativity (90%) were frequently observed. These findings are consistent with international reports on MM immunophenotype and support the utility of flow cytometry in diagnosis and risk stratification [22]. Light chain restriction analysis showed a predominance of kappa light chain (62%), in line with earlier South Asian data [14].

Among cytogenetic abnormalities, gain of 1q21 (20%), del(17p13) (18%), and t(4;14) (14%) were the most frequent. These alterations are known to confer poor prognosis and are often associated with high-risk MM, particularly del(17p13), which involves the TP53 tumor suppressor gene [20, 23]. Notably, nearly half of the patients had normal cytogenetics, emphasizing the limitation of conventional cytogenetics and the need for more sensitive techniques like FISH and next-generation sequencing [24, 25].

The Revised International Staging System (R-ISS) distribution in our cohort revealed that nearly 80% of patients presented with intermediate to high-risk disease (Stage II or III). This is comparable to findings by Kim *et al*. and Hanbali *et al*., who showed that serum albumin, β2-microglobulin, and LDH levels are strongly associated with staging and overall prognosis [23, 26]. Our findings of hypoalbuminemia and elevated LDH reinforce these associations.

In comparison to international studies, such as those by Gerecke *et al*. and Dutoit *et al*., who highlight the role of early and integrated diagnostic approaches including imaging and molecular profiling, our study underscores the diagnostic gap in resource-limited settings where access to MRI, PET-CT, and comprehensive cytogenetics is often restricted [27, 28]. This delay in diagnosis may explain the higher proportion of advanced-stage disease and aggressive morphological patterns observed.

The results of this study support the urgent need for enhanced diagnostic infrastructure, earlier screening in high-risk populations, and broader access to immunophenotyping and cytogenetic tools in Bangladesh. Moreover, the findings highlight the importance of combined evaluation through clinical, biochemical, morphological, and molecular parameters, as emphasized by Štifter *et al*. and Caers *et al*. [18, 22].

Limitations of the study

This study was conducted at a single tertiary care center with a relatively small sample size, which may limit the generalizability of the findings. Advanced diagnostic modalities such as FISH, next-generation sequencing, and functional imaging (e.g., PET-CT) were not uniformly available, potentially underestimating the cytogenetic and disease burden. Additionally, the cross-sectional design precludes assessment of treatment outcomes and survival, which are essential for evaluating long-term prognostic indicators.

CONCLUSION

In conclusion, our study provides valuable insights into the baseline characteristics and risk profiles of MM patients in Bangladesh. The predominance of intermediate to high-risk disease at presentation, along with adverse morphological and cytogenetic features, underscores the need for early detection strategies and risk-adapted therapeutic interventions. Future prospective studies incorporating advanced imaging, minimal residual disease (MRD) assessment, and long-term outcome data will be essential to improve MM care in this region.

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REFERENCES

1. Rajkumar SV. Multiple myeloma: 2018 update on diagnosis, risk-stratification, and management. American journal of hematology. 2018 Aug;93(8):1091-110.
2. Kumar SK. Rajkumar v, Kyle RA, *et al*. Multiple myeloma. Nat Rev Dis Primers. 2017;3(1):17046.
3. Rajkumar SV, Dimopoulos MA, Palumbo A, Blade J, Merlini G, Mateos MV, Kumar S, Hillengass J, Kastritis E, Richardson P, Landgren O. International Myeloma Working Group updated criteria for the diagnosis of multiple myeloma. The lancet oncology. 2014 Nov 1;15(12):e538-48.
4. Avet-Loiseau H, Attal M, Moreau P, Charbonnel C, Garban F, Hulin C, Leyvraz S, Michallet M, Yakoub-Agha I, Garderet L, Marit G. Genetic abnormalities and survival in multiple myeloma: the experience of the Intergroupe Francophone du Myelome. Blood. 2007 Apr 15;109(8):3489-95.
5. Kim DS, Yu ES, Kang KW, Lee SR, Park Y, Sung HJ, Choi CW, Kim BS. Myeloma prognostic index at diagnosis might be a prognostic marker in patients newly diagnosed with multiple myeloma. The Korean journal of internal medicine. 2016 Nov 4;32(4):711.
6. Goldschmidt N, Zamir L, Poperno A, Kahan NR, Paltiel O. Presenting signs of multiple myeloma and the effect of diagnostic delay on the prognosis. The Journal of the American Board of Family Medicine. 2016 Nov 1;29(6):702-9.
7. Al Saleh AS, Parmar HV, Visram A, Muchtar E, Buadi FK, Go RS, Dispenzieri A, Kapoor P, Warsame R, Lacy MQ, Dingli D. Increased bone marrow plasma-cell percentage predicts outcomes in newly diagnosed multiple myeloma patients. Clinical Lymphoma Myeloma and Leukemia. 2020 Sep 1;20(9):596-601.
8. Chowdhury MR. A clinical and laboratory profile of multiple myeloma. Journal of Enam Medical College. 2018 Oct 28;8(3):159-64.
9. Choudhury S, Sultana TA, Islam MS, Islam MA, Khanam PA. Multiple Myeloma-A hospital based cross sectional study in Bangladesh. Journal of the Asiatic Society of Bangladesh, Science. 2012;38(2):189-98.
10. Lee N, Lee H, Moon SY, Sohn JY, Hwang SM, Yoon OJ, Youn HS, Eom HS, Kong SY. Adverse prognostic impact of bone marrow microvessel density in multiple myeloma. Annals of Laboratory Medicine. 2015 Sep 1;35(6):563.

11. Michels TC, Petersen KE. Multiple myeloma: diagnosis and treatment. American family physician. 2017 Mar 15;95(6):373-83A.
12. Bladé J, Dimopoulos M, Rosiñol L, Rajkumar SV, Kyle RA. Smoldering (asymptomatic) multiple myeloma: current diagnostic criteria, new predictors of outcome, and follow-up recommendations. Journal of clinical oncology. 2010 Feb 1;28(4):690-7.
13. Sharmin M, Islam MM, Aziz A, Shah S, Rahman MJ, Kabir AA, Kabir AL, Hasan MR, Rahman F, Kabir SH, Azad KA. Efficacy of Bortezomib plus dexamethasone as a first line treatment in newly diagnosed cases of Multiple Myeloma: A Single Centre Study in a Tertiary Care Hospital. Journal of Dhaka Medical College. 2019;28(1):34-41.
14. Sultan S, Irfan SM, Parveen S, Ali H, Basharat M. Multiple Myeloma: A retrospective analysis of 61 patients from a tertiary care center. Asian Pacific Journal of Cancer Prevention. 2016;17(4):1833-5.
15. Madu AJ, Ocheni S, Nwagha TA, Ibegbulam OG, Anike US. Multiple myeloma in Nigeria: An insight to the clinical, laboratory features, and outcomes. Nigerian journal of clinical practice. 2014 Mar 27;17(2):212-7.
16. Basit A, Siddiqui N, Hameed A, Muzaffar N, Athar S. Factors affecting outcome of patients with multiple myeloma. Journal of Ayub Medical College Abbottabad. 2014 Sep 1;26(3):376-9.
17. Firth J. Haematology: multiple myeloma. Clinical Medicine. 2019;19(1):58-60.
18. Štifter S, Babarović E, Valković T, Seili-Bekafigo I, Štemberger C, Načinović A, Lučin K, Jonjić N. Combined evaluation of bone marrow aspirate and biopsy is superior in the prognosis of multiple myeloma. Diagnostic pathology. 2010 Dec;5:1-7.
19. Moulopoulos LA, Dimopoulos MA, Kastritis E, Christoulas D, Gkotzamanidou M, Roussou M, Koureas A, Migkou M, Gavriatopoulou M, Eleutherakis-Papaiakovou E, Gika D. Diffuse pattern of bone marrow involvement on magnetic resonance imaging is associated with high risk cytogenetics and poor outcome in newly diagnosed, symptomatic patients with multiple myeloma: a single center experience on 228 patients. American journal of hematology. 2012 Sep;87(9):861-4.
20. Hose D, Rème T, Hielscher T, Moreaux J, Messner T, Seckinger A, Benner A, Shaughnessy Jr JD, Barlogie B, Zhou Y, Hillengass J. Proliferation is a central independent prognostic factor and target for personalized and risk-adapted treatment in multiple myeloma. Haematologica. 2010 Sep 30;96(1):87.
21. Manier S, Sacco A, Leleu X, Ghobrial IM, Roccaro AM. Bone marrow microenvironment in multiple myeloma progression. BioMed Research International. 2012;2012(1):157496.
22. Caers J, Garderet L, Kortüm KM, O'Dwyer ME, van de Donk NW, Binder M, Dold SM, Gay F, Corre J, Beguin Y, Ludwig H. European Myeloma Network recommendations on tools for the diagnosis and monitoring of multiple myeloma: what to use and when. haematologica. 2018 Aug 31;103(11):1772.
23. Hanbali A, Hassanein M, Rasheed W, Aljurf M, Alsharif F. The evolution of prognostic factors in multiple myeloma. Advances in hematology. 2017;2017(1):4812637.
24. Landgren O, Rajkumar SV. New developments in diagnosis, prognosis, and assessment of response in multiple myeloma. Clinical Cancer Research. 2016 Nov 15;22(22):5428-33.
25. Perrot A, Lauwers-Cances V, Corre J, Robillard N, Hulin C, Chretien ML, Dejoie T, Maheo S, Stoppa AM, Pegourie B, Karlin L. Minimal residual disease negativity using deep sequencing is a major prognostic factor in multiple myeloma. Blood, The Journal of the American Society of Hematology. 2018 Dec 6;132(23):2456-64.
26. 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. Annals of hematology. 2010 Apr;89:391-7.
27. Gerecke C, Fuhrmann S, Strifler S, Schmidt-Hieber M, Einsele H, Knop S. The diagnosis and treatment of multiple myeloma. Deutsches Ärzteblatt International. 2016 Jul 11;113(27-28):470.
28. Dutoit JC, Verstraete KL. MRI in multiple myeloma: a pictorial review of diagnostic and post-treatment findings. Insights into imaging. 2016 Aug;7:553-69.