

## Bone Involvement in Multiple Myeloma: A Study of Skeletal Deformities in Newly Diagnosed Cases

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### Abstract

**Background:** Multiple myeloma (MM) is a hematologic malignancy commonly associated with skeletal involvement, including bone pain, fractures, and deformities. Bone-related complications significantly impact patients' quality of life. However, the extent of skeletal deformities in newly diagnosed MM patients in Bangladesh remains underexplored.

**Methods:** A retrospective observational study was conducted at BSMMU and private hospitals from April 2023 to March 2024. A total of 48 newly diagnosed MM patients were included. Clinical parameters such as age, gender, hemoglobin level, serum calcium, and renal function were recorded. Skeletal deformities were classified as vertebral collapse, lytic lesions, pathological fractures, bone pain, or other. Treatment outcomes and associations with clinical parameters were also analyzed.

**Result:** The study population had a mean age of  $58 \pm 8.5$  years, with 62.5% male and 37.5% female patients. Common skeletal deformities included bone pain (87.5%), lytic lesions (62.5%), and vertebral collapse (41.7%). Clinical parameters such as low hemoglobin, elevated serum calcium, renal dysfunction, and advanced disease stage were significantly associated with skeletal deformities ( $p < 0.05$ ). After treatment, 79.2% of patients showed improvement in bone pain, and 62.5% had stabilization of fractures. However, 20.8% showed progression of deformities, and 16.7% died during follow-up.

**Conclusion:** Skeletal deformities are prevalent and significantly affect the quality of life in newly diagnosed MM patients. Early diagnosis, effective management, and improved imaging techniques are crucial in mitigating these complications, particularly in low socio-economic settings like Bangladesh.

**Keywords:** Multiple myeloma, skeletal deformities, bone pain, lytic lesions, vertebral collapse.

### 1. INTRODUCTION

Multiple myeloma (MM) is a hematological malignancy characterized by the uncontrolled proliferation of plasma cells in the bone marrow, leading to various systemic complications.<sup>1</sup> While relatively rare, MM is a serious condition primarily affecting older adults, with a median age of diagnosis around 70 years.<sup>2</sup> One of the defining features of MM is its involvement of the skeletal system, affecting over 80% of patients.<sup>3</sup> Skeletal complications such as bone pain, fractures, and skeletal deformities significantly contribute to the morbidity and reduced quality of life in patients.<sup>4</sup>

Bone involvement in MM arises from the interaction between myeloma cells and the bone microenvironment, resulting in an imbalance between bone resorption and formation.<sup>2</sup> Myeloma cells secrete factors that stimulate osteoclast activity, leading to bone destruction and the formation of osteolytic lesions.<sup>5,6</sup> These lesions are most commonly found in areas with high marrow activity, such as the vertebrae, ribs, and pelvis.<sup>3</sup> In addition to osteolytic lesions, patients often experience pathological fractures and vertebral collapses, which exacerbate pain and functional impairments.<sup>7</sup>

The clinical manifestations of skeletal deformities in MM patients can range from mild

bone pain to severe fractures that result in permanent disability.<sup>8</sup> This leads to a marked decrease in mobility, further increasing the risk of complications such as deep vein thrombosis, infections, and immobility-related comorbidities.<sup>9</sup> Skeletal involvement is also associated with an increased risk of spinal cord compression, which can cause neurological deficits and require emergency intervention.<sup>10</sup> Furthermore, vertebral fractures and deformities may also lead to height loss and abnormal spinal curvature, which significantly affect the patient’s posture and daily activities.<sup>8</sup>

In Bangladesh, the incidence of multiple myeloma increases with age, yet the prevalence and impact of skeletal deformities in Bangladeshi patients remain poorly understood.<sup>11</sup> The clinical presentation of MM in Bangladesh is often complicated by delayed diagnoses, limited access to advanced imaging techniques, and difficulties in managing bone-related complications.<sup>12</sup> Despite these challenges, comprehensive studies focusing on skeletal deformities in newly diagnosed MM patients in Bangladesh are scarce.<sup>13</sup> Therefore, there is a significant gap in understanding the full extent of skeletal involvement in this population. Early detection and appropriate management of skeletal complications are crucial in improving the overall prognosis and quality of life for these patients.<sup>14</sup>

The objective of this study was to investigate the prevalence and types of skeletal deformities in newly diagnosed multiple myeloma patients in Bangladesh.

**2. METHODOLOGY & MATERIALS**

This retrospective observational study was conducted at the Haematology Department of Bangabandhu Sheikh Mujib Medical University (BSMMU) and other private hospitals in Dhaka, Bangladesh, from April 2023 to March 2024. A

**3. RESULT**

**Table1.** Baseline Characteristics of Study Population (N = 48)

Characteristics	Frequency	Percentage (%)
Age (mean ± SD)	58 ± 8.5 years	
Gender		
- Male	30	62.5
- Female	18	37.5
Duration of symptoms	6.2 ± 3.1 months	
Hemoglobin level (<10 g/dL)	36	75.0
Serum calcium (>11 mg/dL)	28	58.3
Serum creatinine (>1.5 mg/dL)	20	41.7

Table 1 presents the baseline characteristics of the study population (N = 48). The mean age of

total of 48 newly diagnosed multiple myeloma patients were included, diagnosed based on clinical evaluation, laboratory investigations, and radiological findings according to the International Myeloma Working Group (IMWG) criteria. Patients with previous skeletal deformities or other known bone disorders unrelated to multiple myeloma were excluded from the study. Data collection was performed retrospectively, recording demographic details, clinical characteristics, laboratory results, and radiological findings.

The primary objective of the study was to assess the types and distribution of skeletal deformities in newly diagnosed multiple myeloma patients. Skeletal involvement was evaluated through imaging techniques, including X-rays and MRI, to identify vertebral collapses, lytic lesions, pathological fractures, and other bone-related deformities. The severity of skeletal deformities was classified based on the imaging results. Blood samples were obtained for routine investigations, including hemoglobin levels, serum calcium, and serum creatinine levels. Renal function was assessed as part of the disease-related complications. A thorough clinical examination was performed to assess any associated symptoms, including bone pain and deformities.

Treatment outcomes were monitored throughout the study period. The patients received standard multiple myeloma therapy, including chemotherapy and supportive care. Clinical improvements in bone pain and skeletal deformities were recorded during follow-up visits. Informed consent was obtained from all patients before participation. Data analysis was performed using SPSS software, with descriptive statistics used to summarize patient characteristics and outcomes. A p-value <0.05 was considered statistically significant.

participants was 58 ± 8.5 years. Males constituted 62.5% of the population, while

females made up 37.5%. The average duration of symptoms was  $6.2 \pm 3.1$  months. Among the participants, 75% had hemoglobin levels below

10 g/dL, 58.3% had serum calcium levels above 11 mg/dL, and 41.7% had serum creatinine levels exceeding 1.5 mg/dL.

**Table2.** *Types and Distribution of Skeletal Deformities (N = 48)*

Type of Deformity	Frequency	Percentage (%)
Vertebral collapse	20	41.7
Lytic lesions	30	62.5
Pathological fractures	15	31.3
Bone pain	42	87.5
Other	5	10.4

Table 2 outlines the types and distribution of skeletal deformities among the study population (N = 48). Bone pain was the most prevalent symptom, reported in 87.5% of patients. Lytic lesions were observed in 62.5% of participants,

followed by vertebral collapse in 41.7% and pathological fractures in 31.3%. Additionally, 10.4% of patients presented with other types of skeletal deformities.

**Table3.** *Association between Clinical Parameters and Skeletal Deformities (N = 48)*

Parameter	With Deformity (n = 42)	Without Deformity (n = 6)	p-value
Hemoglobin level (<10 g/dL)	34	2	0.02*
Elevated serum calcium (>11)	25	3	0.03*
Renal dysfunction	18	2	0.04*
Advanced stage disease	40	2	<0.01**

Table 3 examines the association between clinical parameters and skeletal deformities in the study population (N = 48). Among patients with skeletal deformities (n = 42), the prevalence of hemoglobin levels below 10 g/dL, elevated serum calcium (>11 mg/dL), and renal dysfunction was significantly higher compared

to those without deformities (n = 6), with p-values of 0.02, 0.03, and 0.04, respectively. Advanced-stage disease was strongly associated with skeletal deformities, observed in 40 out of 42 patients with a p-value of <0.01, indicating a highly significant correlation.

**Table4.** *Treatment Outcomes (N = 48)*

Outcome	Frequency	Percentage (%)
Improvement in bone pain	38	79.2
Stabilization of fractures	30	62.5
Progression of deformities	10	20.8
Mortality during follow-up	8	16.7

Table 4 summarizes the treatment outcomes among the study population (N = 48). A significant proportion of patients (79.2%) reported improvement in bone pain following treatment, while 62.5% experienced stabilization of fractures. However, 20.8% showed progression of skeletal deformities, and 16.7% of patients succumbed during the follow-up period.

**4. DISCUSSION**

Multiple myeloma (MM) is a plasma cell malignancy that disrupts normal bone homeostasis, leading to significant skeletal complications. This study explored baseline characteristics, skeletal deformities, associated clinical parameters, and treatment outcomes in newly diagnosed MM patients in a Bangladeshi cohort, shedding light on the disease burden and management challenges in a resource-limited setting.

Bone disease is a defining feature of MM, present in more than 80% of patients, and is primarily driven by myeloma cell activity on the bone microenvironment. These cells secrete osteoclast-activating factors, including receptor activator of nuclear factor kappa-B ligand (RANKL), leading to enhanced bone resorption and suppressed bone formation. This imbalance results in lytic lesions, pathological fractures, and vertebral collapses, as highlighted in studies by Callander and Roodman.<sup>15</sup> In our study, lytic lesions (62.5%), vertebral collapses (41.7%), and pathological fractures (31.3%) were consistent with the global prevalence, while bone pain was the most common symptom (87.5%), corroborating findings by Rasch.<sup>16</sup>

The clinical burden of MM-related bone disease is exacerbated in resource-limited settings like Bangladesh, where diagnostic delays are

common. Advanced imaging techniques, such as PET/CT and whole-body MRI, have been shown to detect bone involvement earlier and with greater accuracy than conventional radiographs.<sup>17</sup> However, in Bangladesh, these modalities remain inaccessible for many patients, leading to delayed diagnoses and advanced disease presentations. Our findings reveal a high prevalence of advanced-stage disease, emphasizing the need for increased awareness and improved diagnostic capabilities.

The association between skeletal deformities and clinical parameters, such as anemia, hypercalcemia, and renal dysfunction, is well-established. In our study, hemoglobin levels  $<10$  g/dL, elevated serum calcium ( $>11$  mg/dL), and renal dysfunction were significantly associated with skeletal deformities ( $p < 0.05$ ). Advanced-stage disease ( $p < 0.01$ ) also correlated strongly with skeletal complications, consistent with studies by Michels and Petersen, who highlighted the systemic impact of MM-related bone disease.<sup>18</sup>

Management of MM-related bone disease is multifaceted, involving systemic therapy, bisphosphonates or RANKL inhibitors, and localized interventions like radiation. Bisphosphonates, particularly zoledronic acid, have demonstrated efficacy in reducing skeletal-related events and improving bone pain. In our cohort, 79.2% of patients reported improvement in bone pain, and 62.5% achieved stabilization of fractures following treatment, reflecting the effectiveness of integrated therapeutic strategies. However, 20.8% of patients experienced disease progression, highlighting the aggressive nature of MM and the challenges in managing advanced skeletal deformities.<sup>19</sup>

Recent advances in MM management include monoclonal antibodies targeting bone microenvironment pathways, such as denosumab, which inhibit osteoclast-mediated bone resorption. Additionally, novel agents like proteasome inhibitors and immunomodulatory drugs have shown promise in improving survival outcomes, particularly when combined with traditional therapies. These advances underline the importance of early diagnosis and tailored treatment to mitigate skeletal complications.<sup>20</sup>

Prognostic implications of skeletal abnormalities in MM are significant. Extensive bone disease is associated with poorer outcomes, as noted by Matsue, who found that

bone marrow abnormalities in the appendicular skeleton negatively impacted prognosis.<sup>21</sup> Similarly, Kristinsson emphasized that bone disease serves as an indicator of disease burden and guides clinical management decisions.<sup>22</sup> Our study aligns with these findings, demonstrating that skeletal deformities are not only a source of morbidity but also a marker of disease severity.

The role of advanced imaging in detecting and monitoring MM-related bone disease cannot be overstated. Whole-body low-dose CT (WBLDCT) and <sup>18</sup>F-FDG PET/CT have been shown to outperform conventional skeletal surveys in identifying bone lesions and predicting disease progression. A study by Hillengass highlighted the superiority of WBLDCT in detecting lytic lesions, leading to more accurate staging and treatment planning.<sup>23</sup> Incorporating such technologies into routine practice in Bangladesh could significantly improve patient outcomes.

### 5. LIMITATIONS OF THE STUDY

This study has some limitations, including a small sample size ( $N = 48$ ), which restricts generalizability, and its retrospective design, which may introduce bias in clinical data. The lack of advanced imaging modalities, such as PET/CT, likely underestimates the extent of skeletal involvement. Additionally, resource limitations constrained access to newer therapeutic options, and the single-region focus may not capture the diversity in MM presentations across different populations.

### 6. CONCLUSION

This study highlights the significant burden of skeletal deformities in newly diagnosed multiple myeloma patients and their association with clinical parameters such as anemia, hypercalcemia, and renal dysfunction. Despite the effectiveness of current treatment strategies in managing bone pain and stabilizing fractures, challenges remain in addressing advanced skeletal complications. The findings underscore the importance of early diagnosis, comprehensive management approaches, and the integration of advanced diagnostic tools to improve patient outcomes. Efforts to bridge resource gaps and develop cost-effective, standardized care pathways are essential to mitigate the impact of MM-related bone disease, particularly in resource-constrained settings.

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