INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

OPEN ACCESS

Review Article

Comprehensive Review on Multiple Myeloma: Pathophysiology, Diagnosis, and Current Treatment Strategies

Dr. B. V. Ramana, K. S. Pradhiyumna*

Dr. K .V. Subba Reddy Institute of Pharmacy, Kurnool

ARTICLE INFO

Published: 10 Aug 2025
Keywords:
Multiple Myeloma, hematological malignancy, abnormal plasma cells, bone marrow, bone lesions, renal dysfunction.
DOI:
10.5281/zenodo.16789251

ABSTRACT

Multiple Myeloma (MM) is a hematological malignancy marked by the proliferation of abnormal plasma cells in the bone marrow, leading to multiple systemic complications including bone lesions, renal dysfunction, and anemia. Despite significant advances in diagnostic and therapeutic methods, MM remains largely incurable, although survival outcomes have improved. This review outlines the disease's etiology, pathogenesis, clinical manifestations, diagnostic techniques, staging systems, and the evolving landscape of treatment approaches, providing a comprehensive summary of the current knowledge base.

INTRODUCTION

Multiple Myeloma is a clonal plasma cell neoplasm that accounts for nearly 10% of all hematologic cancers. The disease primarily affects older adults and is characterized by the uncontrolled production of monoclonal immunoglobulins (M-proteins), leading to bone marrow infiltration, immune suppression, and end-organ damage. The emergence of novel agents and improved supportive care have revolutionized the management of MM, shifting the prognosis from terminal to chronic in many cases.

EPIDEMIOLOGY

MM predominantly affects individuals over the age of 60, with a slightly higher incidence in males and African-American populations. Globally, approximately 160,000 new cases are diagnosed each year. Improvements in diagnostic capabilities have led to earlier recognition of asymptomatic or smoldering MM, contributing to better disease surveillance.

ETIOLOGY AND RISK FACTORS :

***Corresponding Author:** K. S. Pradhiyumna
Address: *Dr. K .V. Subba Reddy Institute of Pharmacy, Kurnool*
Email : pradhiyumna522@gmail.com
Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

The exact cause of MM remains unclear, but genetic mutations, chromosomal abnormalities (such as translocations involving chromosome 14), and environmental exposures (like radiation or benzene) are implicated. Risk factors include advanced age, family history, male gender, obesity, and certain occupational exposures.

PATHOPHYSIOLOGY

The disease originates from a malignant transformation of post-germinal center B-cells into monoclonal plasma cells. These cells proliferate in the bone marrow and secrete large amounts of M-protein. This leads to immune dysfunction, osteolytic bone destruction via cytokine release (particularly IL-6 and RANKL), hypercalcemia, anemia due to marrow suppression, and renal failure secondary to light chain deposition.

CLINICAL FEATURES

SYMPTOMS Of Mm Are Often Nonspecific and Develop GRADUALLY:

- Bone pain (commonly in the back or ribs)
- Fatigue and anemia
- Recurrent infections
- Renal insufficiency
- Hypercalcemia symptoms like nausea, constipation, and confusion
- Pathological fractures

DIAGNOSIS

Diagnosis is based on the CRAB criteria (Calcium elevation, Renal dysfunction, Anemia, Bone lesions) along with:

- Serum and urine protein electrophoresis
- Immunofixation
- Free light chain assay
- Bone marrow biopsy (>10% clonal plasma cells)
- Imaging studies (X-ray, MRI, PET-CT)
- Cytogenetic and molecular studies provide additional prognostic information.

STAGING

Two main systems are used:

1. International Staging System (ISS) – based on serum beta-2 microglobulin and albumin.
2. Revised-ISS (R-ISS) – includes cytogenetic abnormalities and LDH levels.

Stage I indicates a favorable prognosis, whereas Stage III suggests a poor outcome.

TREATMENT

Treatment decisions are guided by disease stage, patient age, renal function, and cytogenetic risk profile.

1. Initial Therapy:

- Induction regimens: Bortezomib, lenalidomide, and dexamethasone (VRd) are commonly used.
- Stem Cell Transplant: Autologous transplantation is standard in eligible patients after induction.
- Usually with lenalidomide to prolong remission.

2. Relapsed/Refractory MM:

Next-generation agents: Carfilzomib, daratumumab, pomalidomide.Emerging options: Bispecific T-cell engagers (BiTEs), CAR T-cell therapy (e.g., ide-cel, cilta-cel).

Supportive treatments include bisphosphonates for bone health, antibiotics, antivirals, erythropoiesis-

stimulating agents, and hydration for renal protection.

RECENT ADVANCES

The introduction of monoclonal antibodies, CAR T-cell therapies, and proteasome inhibitors has dramatically changed the treatment landscape. Ongoing trials are exploring the utility of combination regimens, novel immunotherapies, and personalized medicine approaches using molecular profiling.

CONCLUSION

Multiple Myeloma remains a complex and heterogeneous disease with evolving diagnostic and treatment paradigms. While curative therapy remains elusive, advances in therapeutic options have significantly enhanced the survival and quality of life of patients. Continued research is essential for developing individualized treatment strategies and discovering curative potential.

REFERENCES

1. Rajkumar SV. Multiple Myeloma: 2024 Update on Diagnosis, Risk-Stratification, and Management. Am J Hematol. 2024.
2. Palumbo A, Anderson K. Multiple Myeloma. N Engl J Med. 2011;364(11):1046–60.
3. Kumar SK et al. Improved survival in multiple myeloma and the impact of novel therapies. Blood. 2008;111(5):2516–20.
4. Landgren O, Rajkumar SV. New developments in diagnosis, prognosis, and assessment of response in multiple myeloma. Clin Cancer Res. 2016;22(22):5428–33.
5. National Comprehensive Cancer Network (NCCN) Guidelines – Multiple Myeloma, Version 1.2025.
6. Sonneveld P et al. Treatment of multiple myeloma with high-risk cytogenetics: A consensus of the International Myeloma Working Group. Blood. 2016;127(24):2955–62.
7. Usmani SZ et al. Emerging therapeutic targets in multiple myeloma. Clin Lymphoma Myeloma Leuk. 2022;22(2):75–82.
8. Moreau P, de Wit E, Mateos MV. Treatment of multiple myeloma in the era of CAR T-cell therapy and bispecific antibodies. Lancet. 2022;400(10359):1066–78.
9. Attal M, Richardson PG, Rajkumar SV, San-Miguel JF, Beksac M, Goldschmidt H, et al. Is multiple myeloma a curable disease? J Clin Oncol. 2021;39(34):3833–45.
10. Mikhael J, Ismaila N, Cheung MC, Costello C, Dhodapkar MV, Kumar S, et al. Treatment of multiple myeloma: ASCO and CCO joint clinical practice guideline. J Clin Oncol. 2019;37(14):1228–63.
11. Munshi NC, Anderson KC. Prognostic factors in multiple myeloma: more than staging. Nat Rev Clin Oncol. 2013;10(10):588–90.
12. Kumar SK, Dimopoulos MA, Kastritis E, et al. Natural history of relapsed myeloma refractory to immunomodulatory drugs and proteasome inhibitors: a multicenter IMWG study. Leukemia. 2017;31(11):2443–8.

HOW TO CITE: Dr. B. V. Ramana, K. S. Pradhiyumna, Comprehensive Review on Multiple Myeloma: Pathophysiology, Diagnosis, and Current Treatment Strategies, Int. J. of Pharm. Sci., 2025, Vol 3, Issue 8, 912-914. https://doi.org/10.5281/zenodo.16789251