ORIGINAL RESEARCH PAPER

Pathology

A STUDY OF CLINICAL PROFILE AND LABORATORY PARAMETER IN MULTIPLE MYELOMA AT SMS MEDICAL COLLEGE & HOSPITAL, JAIPUR

KEY WORDS: Bone marrow , multiple myeloma , plasma cell

Dr.Deepika Mishra Professor ,Department Of Pathology SMS Medical College &Hospital Jaipur.

Dr Gayatri Meena* Junior Resident, Department Of Pathology SMS Medical College &Hospital Jaipur. *Corresponding Author

Dr Sapna Gandhi Associate Professor, Department Of Pathology SMS Medical College & Hospital Jaipur.

Dr Kanta Prasad Consultant Orthopaedics, Apex Ranthambhor Sevika.

ABSTRACT

Introduction: Myeloma is characterized by the neoplastic proliferation of a single plasma cell of terminally differentiated B lymphoid cells that produces monoclonal immunoglobulin. Myeloma often manifests with many clinical symptoms and organ damage, including anemia, hypercalcemia, renal insufficiency, lytic bone lesion, hyperviscosity, amyloidosis, and infection.

Background : Bone marrow examination gold standard in establishing the diagnosis of multiple myeloma along with clinical ,radiological and laboratory parameters the histological criteria for staging will help in determining the prognosis.

Objective: To correlate the clinical and laboratory parameter in the diagnosis and staging of multiple myeloma in the SMS Medical College & Hospital Jaipur.

Materials and Methods: All haematological sample of multiple myeloma and histopathology specimens received of respective tissues in Department of Pathology SMS Medical College & Attached Hospital, Jaipur. Study from 2019 to 2020.

Results : 49 patients were included in this study. The mean age was 59.08 years. Male :female ratio 1.6:1.Most common clinical presentation weakness. The most common morphologic type of MM was mature myeloma followed by plasmablastic and immature type accounting 60%,24%, 16% each. Amongst the variable hemoglobin ,serum creatinine ,serum urea, and presence of bone lesion in single or multiple site were found to be statistically significant.

Conclusion: The present study highlight correlation between clinical presentation, radiological findings and laboratory parameters establishing the diagnosis of multiple myeloma. The present study has application of Durie-Salmon criteria and its staging system in the limited resources setting for diagnosis. Bone marrow aspiration and biopsy help in establishing diagnosis of multiple myeloma. The existence of two Staging System DSS & ISS with no mutually common parameters raises the possibility that they both are valid in differing situation and are tools for diagnosis of multiple myeloma.

INTRODUCTION

Myeloma is characterized by the neoplastic proliferation of a single plasma cell of terminally differentiated B lymphoid cells that produces monoclonal immunoglobulin. It account for 1% of all malignant diseases and about 10% of hematological malignancies. In most cases neoplastic plasma cell proliferation in the bone marrow and result in extensive skeletal destruction with osteolytic lesions. Myeloma often manifests with many clinical symptoms and organ damage, including cytopenias, anemia, hypercalcemia, renal insufficiency, lytic bone lesion, hyperviscosity, amyloidosis, and infection. Based on classification and diagnostic criteria proposed by the International Myeloma Working Group (IMWG), the diagnosis of myeloma is based on the level of M-protein in the serum and or urine, rate of clonal plasma cells in the bone marrow, and the presence of organ damage. However it is important to determine precisely whether proliferative plasma cell in the bone marrow are neoplastic by pathological diagnosis .The hallmark of myeloma is the increase monoclonal plasma cell which vary from 10% to 90%.[1]

A combination of radiological, laboratory, pathological findings provides the diagnosis of MM. Diagnosis of MM according to Durie - Salmon has major and minor criteria.[2] Recent technological advance like MRI immune - phenotyping, FISH and marker like beta-2 microglobulin and serum IL6 level estimated has come to the picture in determining the prognosis.[3] However, quantifying the volume of plasma cell infiltration and assessing the degree of plasma cell dysplasia in the bone marrow aspirate and trephine biopsy is still remains the gold standard.[4] Low platelet count are frequently observed in MM due to infiltration of the marrow by plasma cell or intravascular destruction of platelets. Count <1000000/ul have been reported.[5,6]

MM cells are similar to post germinal center (GC) long-lived PCs, characterized by strong BM dependence, extensive somatic hypermutation (SHM) of immunoglobulin (Ig) genes, and absence of IgM expression in all but present in 1% of tumors.[7]

Many studied show that various histological parameter also a definite prognostic significance and they are : degree of plasma cell atypia, the extent of marrow infiltration by the myeloma cells, pattern of growth of the neoplastic clone ,marrow fibrosis and mitotic index.[8,9,10]

AIM

- To study clinical and laboratory findings of patient with multiple myeloma.

OBJECTIVES

- To study the age and gender occurrence and common modes of clinical presentation of multiple myeloma.
- To study the clinical presentation and laboratory parameters in patients diagnosed with multiple myeloma and apply the International Multiple Myeloma Working Group criteria in diagnostic and prognostic evaluation in comparison with Durie and Salmon criteria.

MATERIALS AND METHODS

Study period : Prospective period was from 2019 to November 2020.

- Clinical and laboratory parameters were recorded, Bone marrow aspiration and bone marrow biopsy samples collected, staining was done with Leishman's, MGG, Haematoxyline & Eosin and Reticulin stain. IHC was done for CD138, Kappa, Lambda as and when required. IMWG and Durie –Salmon criteria were applied for diagnosis and patients were staged in accordance with Durie –Salmon staging system.(based on Hb ,serum calcium, serum creatinine,serum electrophoresis, skeletal imaging).

- **Study period :** Prospective period was from 2019 to November 2020.
- Clinical and laboratory parameters were recorded, Bone marrow aspiration and bone marrow biopsy samples collected, staining was done with Leishman's, MGG, Haematoxyline & Eosin and Reticulin stain. IHC was done for CD138, Kappa, Lambda as and when required. IMWG and Durie –Salmon criteria were applied for diagnosis and patients were staged in accordance with Durie –Salmon staging system.(based on Hb ,serum calcium, serum creatinine,serum electrophoresis, skeletal imaging).

INCLUSION CRITERIA:

1. Bone Marrow Aspirate and biopsy of patient suspicious of multiple myeloma by clinical history and examination.
2. Cellularity present in received specimen.
3. Properly formalin fixed biopsy and bone marrow aspirate specimen.

EXCLUSION CRITERIA:

1. The patients profile not fitting with diagnostic criteria in spite of clinical history.
2. Patient suspicious of monoclonal gammapathy of undetermined significance.

Data Management and statistical analysis

RESULT AND OBSERVATION

With due consideration of all inclusion and exclusion criteria total 49 patients were included in the study

Clinical presentation –

Age –The age presentation ranged from 21 to 80 years with an average age of 59.08 years. The highest peak (43%) 21 patients were aged between 61-70 years and followed by (19%) 9 patients are 71 -80 year of age least common (6%) 3 patients of 21 -30 year age.

Gender –The male to female ratio was 1.6: 1 with male predominance. 30 patients were males (61%) and 19 (39%) were females.

Clinical presentation	Number	Percentage
Weakness	26	53%
Backache	25	51%
Bone tenderness	14	29%
Fever	13	27%
Blood transfusion	6	12%
Bleeding	2	4%
CKD	2	4%
Chest pain	1	2%
CML	1	2%
Epistaxis	1	2%
Fracture	1	2%
Hepatomegaly	1	2%
Vomiting	1	2%

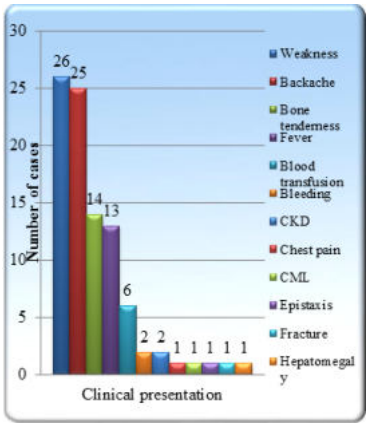


Table & Column chart showing clinical presentations in the study population.

Parameter	Number	Percentage
Calcium ≥ 11mg/dl	10	20%
Creatinine >2mg/dl	19	39%
Hb<10gm/dl	39	80%
Lytic lesion	45	91%

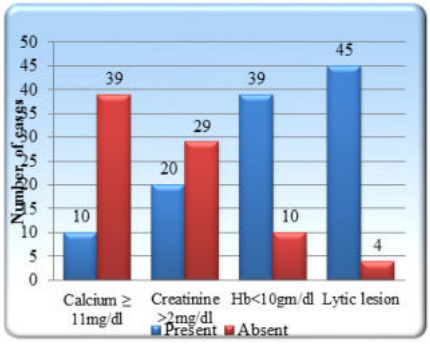
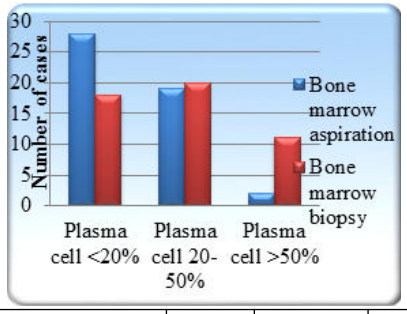


Table &Column chart showing presence of CRAB (Hypercalcemia, renal insufficiency, anemia, bone lesion) in the study population.

In our study, cellularity was normal in 92% of bone marrow aspiration sample and 82% of bone marrow biopsy sample. Hypercellularity was detected in 8% of bone marrow aspiration sample and 18% of bone marrow biopsy sample. There was no significant difference in cellularity among two type of samples (p value 0.234).

Plasma cell (%)	Bone marrow aspiration	Bone marrow biopsy	P value
<20%	28 (57%)	18 (37%)	0.043
20 - 50%	19 (39%)	20 (41%)	0.836
>50%	2 (4%)	11 (22%)	0.017

Table & coloumn chart showing Plasma cell (%) in bone marrow specimen



Plasma cell morphology	Mature	Immature	Plasmablastic
Number of cases (n=49)	29	8	12
Percentage	60%	16%	24%

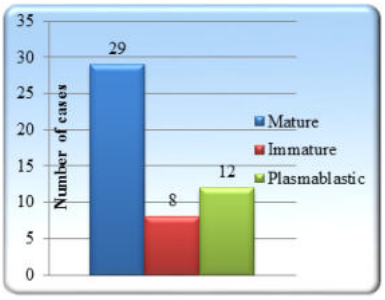


Table & coloumn chart showing Plasma cell morphology type in bone marrow specimen

Parameter		Plasmablastic (n=12)	Mature type (n=29)	Immature type (n=8)	P value
Hematopoiesis	Normal	4 (33%)	25 (86%)	5(62%)	0.002
	Suppressed	8 (67%)	4 (14%)	4(38%)	
Plasma cells	<20%	7 (58%)	18 (62%)	2(25%)	0.193
	20-50%	3 (25%)	10 (34%)	4(50%)	0.536
	>50%	2 (17%)	1 (4%)	2(25%)	0.094
Pattern of infiltration	Diffuse/packed	9 (75%)	1 (3%)	0(0%)	<0.001
	Focal/nodular	2 (17%)	3 (10%)	6(75%)	<0.001
	Interstitial	1 (8%)	25(86%)	2(25%)	

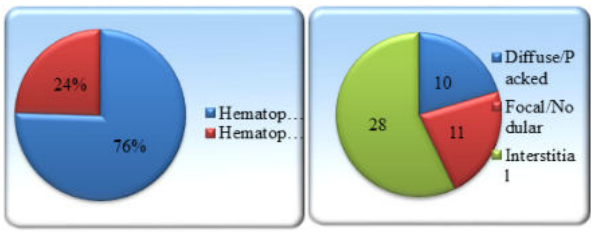
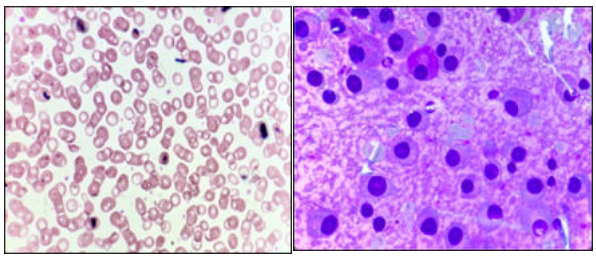
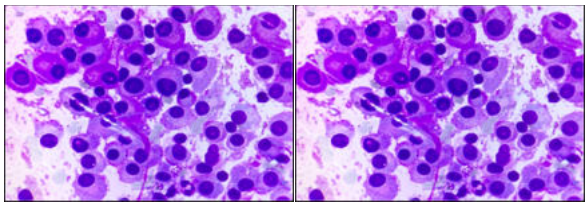


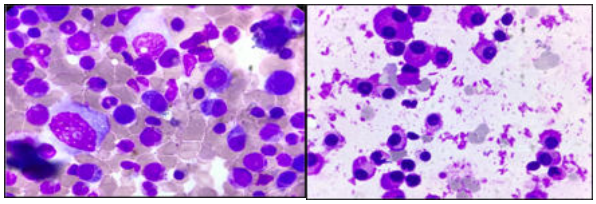
Table &pie chart showing Comparison of different type bone marrow parameters in of mature myeloma, immature myeloma and plasmablastic myeloma



Picture shows Rouleaux formation | **picture shows flame cells**



shows Mature Plasmacytic Cell | **picture shows Immature & PlasmaBlastic Cell**



Picture shows Russell body | **picture shows Binucleated plasma cell**

Bone marrow aspiration showing different types cell

DISCUSSION

Multiple myeloma is a disease resulting from proliferation in the bone marrow of neoplastic B cells that are closely related both morphologically and functionally to plasma cells. It constitutes10-15% of all hematological malignancy. This malignancy usually presents in elderly with a median age in India 56-60 years. Age at presentation ranged from 21 to 80 years with a mean age 59.08 year.

Anemia in Multiple myeloma is due to replacement of marrow by myeloma cells and decreased production of erythropoietin due to accompanying renal involvement in some case it may be associated with cytokine mediated Bone marrow suppression. In our study Anemia was seen in 80% our patients. Rouleaux formation was seen in 57% of our patients which was lower in comparison to observation by Kaushik et al[11] (70%) ,Subramanian R et al [8](91%) ,and Kaur et al [12](82%) ,though higher than Diwan et al[13] r studied Kyle RA[14] (73%).

Thrombocytopenia in our patients (12%) was higher than Diwan et al[13](10%) and Kyle et al[14] (5%) and lower than kaushik et al[11] (24%), kaur et al [12](25%) studied. Serum creatinine more than >2mg/dl significant renal failure which is a serious complication of multiple myeloma.

The mean blood urea level was 62.94mg/dl in our patients is similar to Yassin AK[15]67.3mg/dl).

Bone marrow examination is the gold standard of the diagnosis of MM along with other clinical and laboratory parameters. Bone marrow examination is a one of the diagnostic criteria of MM, Plasma cell %, Plasma Cell morphology and infiltration pattern is of help in prognosis of disease.[8,]

In our study plasmacytic/ mature morphology was more common than plasmablastic. In majority of cases with plasmablastic morphology had diffuse/ packed pattern infiltration 75% followed by focal and interstitial pattern while most common pattern in plasmacytic/mature myeloma was interstitial pattern (86%) followed by focal /nodular and diffuse pattern. Compare other studied Maria freances B[19] Diffuse infiltration in plasmablastic (43.8%), and interstitial pattern in plasmacytic myeloma.

Morphological type of myeloma

Study	No of case	Mature myeloma	Intermediate myeloma	Immature myeloma	Plasmablastic myeloma
Griepp et al [16]1985	100	28%	38%	19%	15%
Carter et al[17] 1987	139	21.6%	-	54.7%	23%
Kuriakose et al [18]1995	89	13.5%	-	59.6%	26.9%
Maria Frances B[19] 2013	70	42.9%	20%	21.4%	15.7%
Sharma et al[20] 2018	50	50%	2%	14%	34%
Present study 2020	49	60%	-	16%	24%

Majority of patients were found in stage III (45%), Stage II (30%), Stage I (25%) compare to other studied in table. Similar to Yassin AK[15] Diwan et al [13]and sharma et al.[20]

When the patients were staged according to Durie-Salmon Staging System anemia was found in our patients 80% of the patients in this series was found with anemia and 41% of them presented with Hb level of less than 8.5gm/dl which included in stage III of Durie-Salmon staging this studied similar to Yassin AK[15].

CONCLUSION

The present study highlight correlation between clinical presentation, radiological findings and laboratory parameters establishing the diagnosis of multiple myeloma. The present study has application of Durie-Salmon criteria and its staging system in the limited resources setting for diagnosis. Bone marrow aspiration and biopsy help in establishing diagnosis of multiple myeloma.

The existence of two Staging System DSS & ISS with no mutually common parameters raises the possibility that they both are valid in differing situation and are tools for diagnosis of multiple myeloma. ISS is easier to compute but as the Beta-2 microglobulin estimation is expensive it is not available in most centres.

REFERENCES

1. Fujino M. The histopathology of myeloma in the bone marrow. J Clin Exp Hematop. 2018;58(2):61-7.
2. Durie BG. Staging and kinetics of multiple myeloma. Semin Oncol. 1986; 13: 300-9.
3. Kyle RA. Diagnosis of multiple myeloma. Semin Oncol. 2002 Dec 17;29(6):2-4.
4. Kyal RA, Gertz MA, Witzing TE, Lust JA, Lacy MQ. Review of 1027 patient with newly diagnosed multiple myeloma Mayo Clin Proc. 2003; 78:21-33.
5. Tripathy S. The role of serum protein electrophoresis in the detection of multiple myeloma: J Clin. Diagn. 2012 Nov ;6(9):1458.
6. Fritz E, Ludwing H, Schiethauer W, Sinzinger H. Shortened platelet half –life in multiple myeloma .Blood. 1986 Aug 1;68(2):514-20.
7. Kuehl WM, Bergsagel PL. Molecular pathogenesis of multiple myeloma and its premalignant precursor. J Clin Invest. 2012 Oct 1;122(10):3456-3.
8. Subramanian R, Basu D, Dutta TK. Prognostic significance of bone marrow histology in multiple myeloma. Indian J Cancer. 2009 Jan 1;46(1):40.
9. Sailer M, Vykoupil KF, Peest D, Coldewey R, Deicher H, Georgii A. Prognostic relevance of a histologic classification system applied in bone marrow biopsies from patients with multiple myeloma: A histopathological evaluation of biopsies from 153 untreated patients. Eur J Haematol. 1995; 54:137-46.
10. Pich A, Chiusa L, Marmount F, Navone R. Risk groups of myeloma patients by histologic pattern and proliferation activity. Am J Surg Pathol. 1997 Mar 1;21:339-47.
11. Kaushik R,Thakur RK, Gulati A ,Sharma KS. Multiple myeloma : clinico-hematological profile in A Tertiary Care Hosp. Ann Lab Med. 2017;4(5): 2394-6466.Mar 1;7(2):185.
12. Kaur P, Shah BS, Baja P. Multiple myeloma: A clinical and pathological profile. Gulf J Oncolog. 2014 Jul;1(16):14-20.
13. Diwan AG, Gandhi SA, Krishna K, Shinde VP. Clinical profile of the spectrum of multiple myeloma in teaching hospital. Med J DY Univ. 2014
14. Kyle RA, Gertz MA, Witzig TE, Lust JA, Lacy, Martha Q et al. Review of 1027 patients with newly diagnosed multiple myeloma. Mayo Clin Proc. 2003;78(1):21-33.
15. Yassin AK. Clinical and Laboratory Profile of 109 Patients diagnosed as Multiple Myeloma in Erbil City. J Fac med Baghdad. 2013 Jul 1;
16. Greipp PR, Raymond NM, Kyle RA, O'Fallon WM. Multiple myeloma: significance of plasmablastic subtype in morphological classification. Blood. 1985;65:305-10. 55(2):121-4.
17. Carter A, Hocherman I, Linn S, Cohen Y, Tatarsky I. Prognostic significance of plasma cell morphology in multiple myeloma. Cancer. 1987 Sep 1; 60(5):1060-5.
18. Kuriakose P, Das S, Mani A. Bone marrow morphology in multiple myeloma. Indian J Cancer. 1995;32(3):100-3.
19. Maria Frances B. Clinicopathological study of multiple myeloma. 2013.
20. Sharma A, Swaroop N, Shashidhar, Karuna RK, Samaga LN, Kishan PH, Sheetty KJ. An analysis of clinical profile and laboratory parameters in multiple myeloma. Indian J Med Res. 2018 March;7 (2):5-15.