Research Article Available online www.ijsrr.org ISSN: 2279–0543

International Journal of Scientific Research and Reviews

Plasma Cell Myeloma – A Three Year Retrospective Study in a Tertiary Care Hospital

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ABSTRACT:

Plasma cell myeloma is known by many names such as Multiple myeloma, myelomatosis and Kahler's disease. It is a rare disorder arising from a monoclonal population of plasma cells producing entire immunoglobulins, fragments of immunoglobulins, heavy and light chanins of immunoglobulins.It can be of two tyes: Secretory and Non-secretory. It has a predilection for older age groups though it can be rarely found in young adults and is more commonly observed in males compared to females. In the current study, we present nine cases of this relatively rare condition which spanned over a period of 2 years. These cases were thouroughly evaluated for the same with all the relevant lab investigations, bone marrow aspiration and biopsy, urine examination and clinic-radiological co-relation. Hemoglobin and Urine Electrophoresis of these patients was done for these cases to confirm our diagnosis which was given on bone marrow examination.

KEYWORDS: Plasma cell myeloma, Multiple myeloma, myelomatosis, Kahler's disease, Secretory myeloma, Non-secretory myeloma, Hemoglobin Electrophoresis, Urine Electrophoresis.

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INTRODUCTION

Plasma Cell Dyscrasias (PCDs) are a broad and extensive spectrum of lasma cell disorders including Monoclonal gammopathy of undetermined significance (MGUS), asymptomatic/ symptomatic Multiple Myeloma (MM), Solitary Plasmacytoma of Bone, Extramedullary Plasmacytoma, Waldenstrom's Macroglobulinaemia (WM), Primary Amyloidosis and Heavy chain Disease [1,2] Plasma Cell Myeloma/ Multiple Myeloma as a term is distinctly characterized by ability of malignant proliferation of population of large numbers of monoclonal plasma cells; which may be accompanied by secretion of monoclonal population of immunoglobulins or paraproteins which are commonly known as M protein, that are secreted in detectable levels in urine, thus known as Secretory Myeloma or may not be accompanied by secretion of M proteins thus known as Non-Secretory Myeloma [1,2].

Multiple Myeloma recorded for **one percent** of all malignancies in the world and 10-20 % of all hematologic malignancies globally[2]. MM still remains an incurable neoplasm of plasma cells with many researches going on for its prompt treatment and cure[2]. Even though it being a rare disease with with very low prevalence, is stands its position as the second most common hematologic malignancy [3].

It is a disease of elderly with predilection for male population over female population [1,2]. It is insidious in its onset, with patients presenting with weakness, weight loss, pallor and fatigue in its early stages [2]. Along with progression of the disease, the patient may resent with recurrent pathological fractures, recurrent infections, coed compresseion with lab investigations showing elevated erythrocyte sedmentation rates, hypercalcemia and deranges renal function tests [2]. All these clinical features are pertaining to skeletal involvement, bone marrow failure, increased viscosity of blood and renal affection by the disease [2].

The distinct trademark features of Multiple myeoma are designated by an "**CRAB**" which stands for Elevated **C**alcium levels, Derranged Renal function tests due to affection of the kidney leading to **R**enal insufficiency, Bone marrow failure leading to **A**nemia and Lytic lesions due the **B**one disease [2,5]. In this era of modernization and quick developments, recent advances and novet technologies are of significant use in recognition of plasma cells pathology. These recent developments consists of Magnetic Resonance Imaging (MRI) of the skeletal bony lesions, detection of the aberrant surface antigens on the plasma cells by Immunophenotyping. FISH (Fluorescent In Situ Hybridization) techniques are along with other molecular techniques are used for characterization of the genetic abnormalities if any [1,4].

MATERIAL AND METHODS

The present study, a retrospective study, consists includes analysis of all cases with clinical suspicion of plasma cell myeloma which presented with increased serum proteins and reversal of Albumin: Globulin ratio; lytic bone lesions, anaemias and elvated erythrocyte sedimentation rates; admitted to the Mahatma Gandhi Medical College and Hospital, Navi-Mumbai during the period from August 2018 to August 2021. Only confirmed cases of Multiple Myeloma are considered in this study. Being a retrospective study, it includes review of clinical, pathological, microbiological and biochemical records of all diagnosed cases of Multiple Myeloma admitted in MGM's Medical college and hospital, Navi Mumbai. A total of nine cases were diagnosed and were confirmed as to cases of Multiple Myeloma using Revised International Myeloma Working

Group diagnostic criteria for multiple myeloma, 2014.

Table 1: Revised International Myeloma Working Group diagnostic criteria for Multiple Myeloma – 2014 [2]

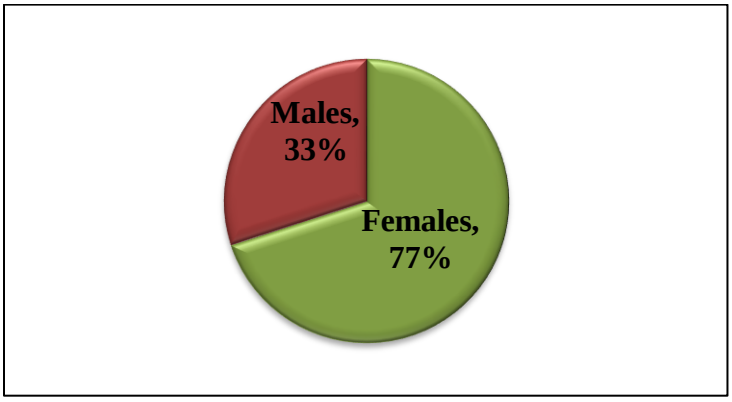
Clonal bone marrow plasma cells 10%or biopsy-proven bony or extramedullary plasmacytoma and any one or more of the following myeloma defining events:
Myeloma defining events: • **Evidence of end organ damage that can be attributed to the underlying plasma cell proliferative disorder, specifically:** - Hypercalcaemia: serum calcium > 0,25 mrnol/L *{* > 1 mg/dL! higher than The upper limit of normal or > 2.75 mmol/1 (> 11 mg/dL) • **Renal insufficiency: creatinine clearance < 40 mlper** minute or serum creatinine > *177* pmot/L (> 2 mg/dL) • **Anaemia: hemoglobin value of > 20 g/L below the** lower limit of normal, or a haemoglobin value of < 100 g/L • **Bone lesions: one or more osteolytic lesions on** skeletal radiography CT or PET
* Any one or more of the following biomarkers of malignancy: • **Clonal bone marrow plasma tell percentage 60%** • **Involved: uninvolved serum free light chain ratio > 100** • **> 1 focal lesions on MRI studies**

As a diagnostic measure, the following laboratory parameters of Multiple Myeloma cases were studied: hemoglobin, hematocrit, leukocyte count, absolute neutrophil count, platelet count, Aspartate transaminase (AST), Alanine transaminase (ALT), lactate dehydrogenase (LDH) anlong with Peripheral Smear examination, Bone Marrow Aspiration and Biopsy.

RESULTS

In the present study, data from a total of nine cases of Multiple Myeloma, confirmed by Bone marrow aspiration and biopsy and confirmed by haemoglobin electrophoresis and urine electrophoresis were analysed and as per the Revised International Myeloma Working Group diagnostic criteria for Multiple Myeloma – 2014.

Figure 1: Sex-wise Distribution of cases



Out of all the nine cases, 7(77%) were females and 2(33%) were males.

Table 2: Age and Sex-wise distribution of Multiple Myeloma cases

Sr.No	Age	Gender
Case 1	75	M
Case 2	45	F
Case 3	65	F
Case 4	66	M
Case 5	55	F
Case 6	60	F
Case 7	60	F
Case 8	63	F
Case 9	54	F

Table 3: Age-wise distribution of Multiple myeloma cases

Age groups	No. of cases	Percentage
41- 50years	01	11%
51- 60 years	04	44%
61-70 years	03	34%
71- 80 years	01	11%

Out of the nine cases, one case each (11%) is found in the age group of 41-50 years and 71-80 years. 4 cases (44%) were in the age group of 51-60years and 3 cases (34%) were found in the age group of 61-70 years.

Thus supporting that Multiple Myeloma shows predilection for the elder age groups.

Figure 2: Age-wise Distribution of cases

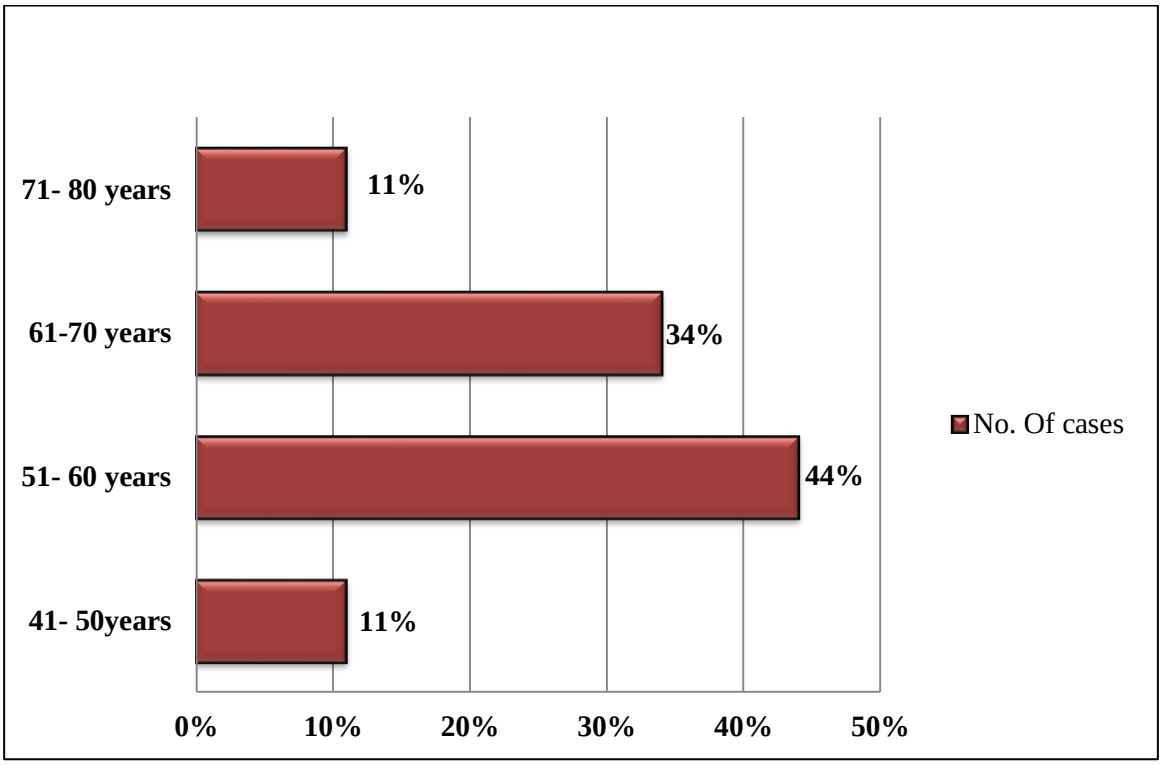


Table 3: Complete Blood Counts (CBC) of Multiple Myeloma cases

Test Parameters	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9
Hb	8.6	7.2	3	6	5.3	6	10.9	7.5	4.8
Tlc	2250	11910	6440	4580	6390	6580	16630	3540	1590
Plt	0.83	1.69	3.67	1.38	0.5	1.28	1.81	0.2	0.37
PCV	23.9	22.2	13	17.6	16.6	17.6	34.2	23	18.2
MCV	114.4	108.3	123.8	89.8	98.9	86.8	87.9	92	62.3
MCH	41.1	35.1	88.6	30.6	31.5	31.6	28	30	16.4
MCHC	36	32.4	71.5	34.1	31.9	32.1	31.9	32.6	26.4
RBC	20.9	2.05	1.05	1.96	1.68	2.96	3.89	2.5	2.92
RDWcv	16.9	14.3	36.8	14	18	14	18.2	15.3	24.2

Out of total of nine cases, eight cases showed Hemoglobin levels below 10 gm/L and a single case had hemoglobin more that 19 gm/L.

Table 4: Liver Function Tests and Serum Calcium Levels of Multiple Myeloma cases

TEST	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9
Total Bilirubin (0.3-1.2 mg/dl)	0.97	0.96	0.96	1.01	0.26	0.88	0.76	0.26	0.25
Direct Bilirubin (00-0.2 mg/dl)	0.06	0.07	0.07	0.27	0.24	0.04	0.07	0.05	0.09
Indirect Bilirubin (0.3-1.0 mg/dl)	0.91	0.89		0.74	0.75	0.72	0.71	0.21	0.22
SGOT (0-50 U/L)	38	40	53	49	33	56	48	33	37
SGPT (0-50U/L)	13	45	52	57	54	47	48	39	47
Alkaline Phosphate (64-300 U/L)	58	56	65	123	79	58	56	58	58
Serum Calcium (mg/dl)	10	11	12	8	13	12	12	14	11

Overall, all these nine cases have Liver Function Tests within normal limits or Sightly raised which are of not great significance.

Table 5: Renal Function Tests of Multiple Myeloma cases

TEST	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9
Creat (0.67-1.17 mg/dl)	3.89	0.92	2.76	8.72	2.09	3.49	2.29	0.6	2.49
Urea (13-43 mg/dl)	41	44	46	181	40	48	42	39	41
Urea Nitrogen (6-20 mg/dl)	19.16	20.8	38.1	84.58	41.1	41.5	40.1	13.6	39.1

Seven out of nine cases have increased Serum Creatinine Levels of more than 2mg/dl.

Of all the nine cases, only one case, that is case number 4 has significantly derranged values of all the tests of renal function as this patient had underlying chronic Kidney disease with timely dialysis going on.

Table 6: Protein levels of Multiple Myeloma cases

TEST	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9
Total Protein (6.6-8.3 g/dl)	10.03	8.08	9.01	7.21	11.09	9.75	9.03	6.53	13.03
Albumin (3.5-5.2 g/dl)	2.08	2.90	2.01	3.5	1.69	2.00	2.08	3.42	3.08
Globulin (2.3-3.5 g/dl)	7.95	5.18	7.00	3.71	9.40	7.95	6.95	3.11	8.95
A/G Ratio (1.2-2.5)	0.26	0.56	0.24	0.94	0.18	0.26	0.26	1.09	0.24

Of all the nine cases of multiple myeloma, 07 cases have increased total protein levels and eight out of nine cases have increased globulin levels. Eight out of nine cases show reversal of Albumin:Globulin ratio.

All these findings along with the other clinical findings raised the clinical suspicion of Multiple Myeloma in these patients.

Table 7: Peripheral Smear (PS) and Bone Marrow Aspiration (BMA) findings of the cases of Multiple Myeloma

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9
Plasma cell (%) on BMA	65%	35%	18%	44%	35%	59%	57%	18%	22%

Bone marrow Aspiration and Biopsy of these cases were done.

All the nine cases show plasma cell percentage on bone marrow aspiration as more than 10% (Defined upperlimit by the Revised International Myeloma Working Group diagnostic criteria for Multiple Myeloma – 2014).

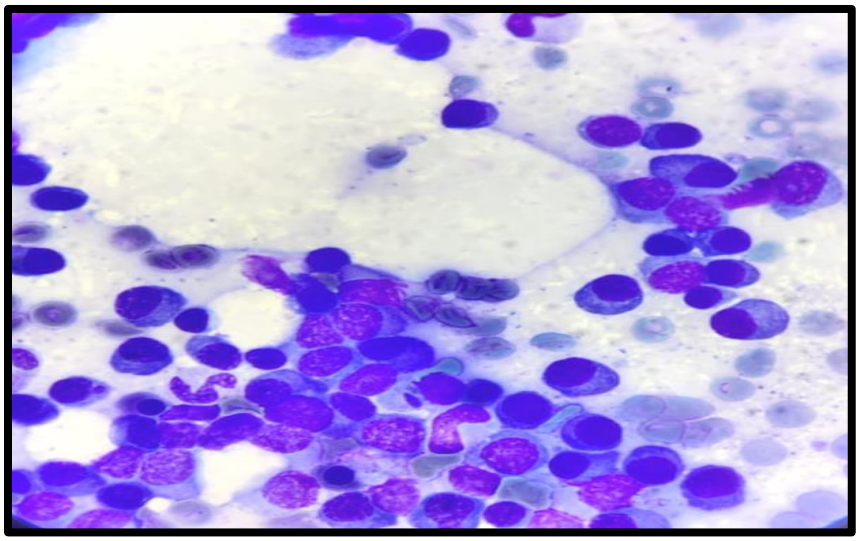


Figure 3: Bone Marrow Aspiration smear showing Plasma cells.

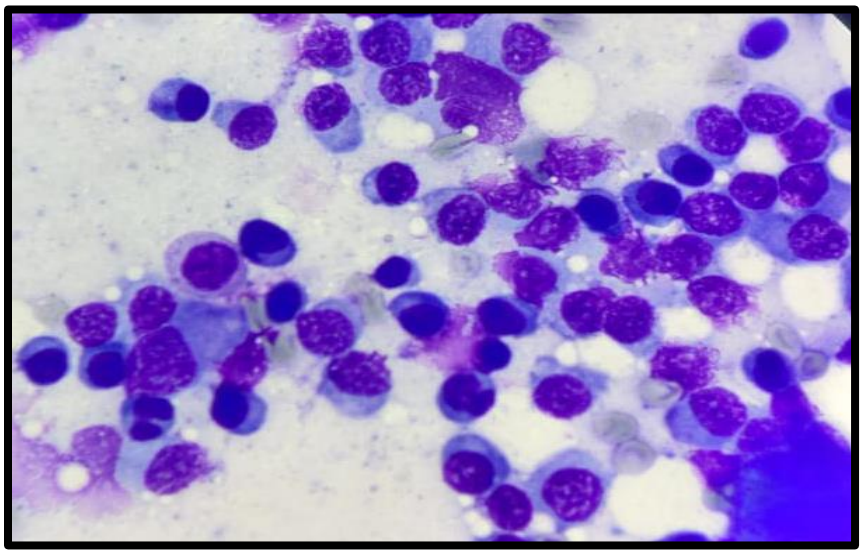


Figure 4: Bone Marrow Aspiration smear showing Plasma cells.

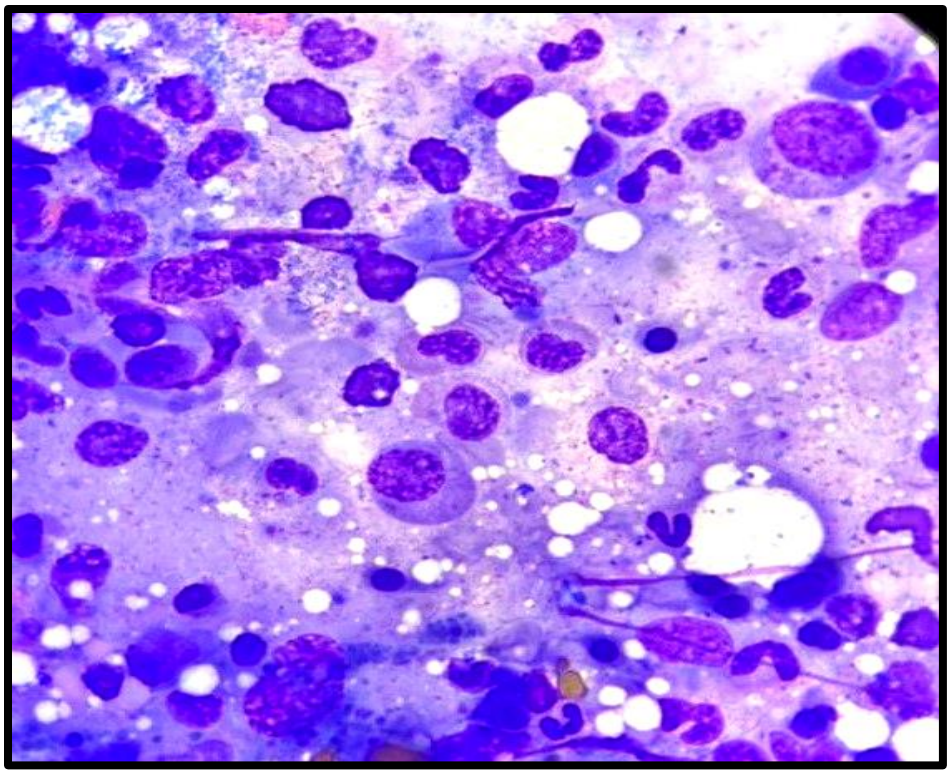


Figure 5: Bone Marrow Aspiration smear showing Plasma cells and Plasmablast.

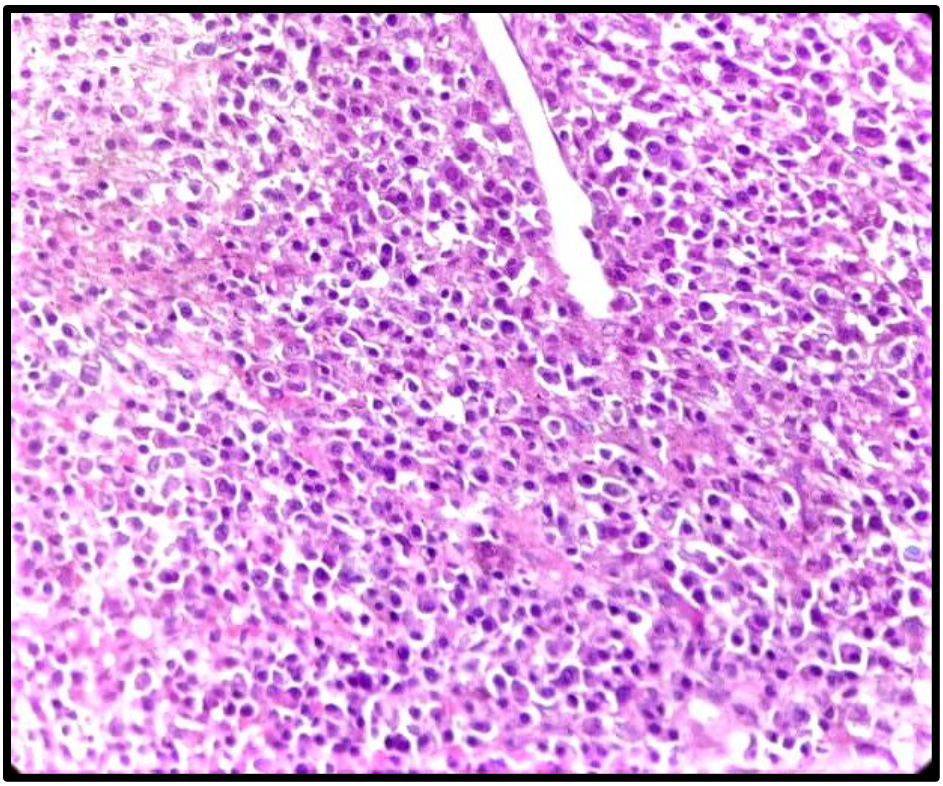


Figure 6: Bone Marrow Biopsy smear showing Plasma cells.

Table 8: Relevant findings of the nine cases of Multiple Myeloma according to Revised International Myeloma Working Group diagnostic criteria for Multiple Myeloma – 2014

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9
Myeloma defining events:									
Serum Calcium Levels	**10**	**11**	**12**	**8**	**13**	**12**	**12**	**14**	**11**
Serum Creatinine Levels	**3.89**	**0.92**	**2.76**	**8.72**	**2.09**	**3.49**	**2.29**	**0.6**	**2.49**
Hemoglobin values	**8.6**	**7.2**	**3**	**6**	**5.3**	**6**	**10.9**	**7.5**	**4.8**
Bone lesions	**Not seen**	**Not seen**	**Noted**	**Noted**	**Noted**	**Noted**	**Not seen**	**Not seen**	**Noted**
Any one or more of the following biomarkers of malignancy:									
Plasma cell (%) on BMA	**65%**	**35%**	**18%**	**44%**	**35%**	**59%**	**57%**	**18%**	**22%**
MRI studies	**Not seen**	**Not seen**	**Not seen**	**Not seen**	**Noted**	**Not seen**	**Noted**	**Not seen**	**Not seen**

As from the above findings, all the cases fulfill the criteria of Plasma Multiple Myeloma with plasma cell percentage of more than 10% along with presence of one or more myeloma defining events. Thus lab diagnosis of Multiple Myeloma was made In these patients.

Further, Urine Bence Jones protein test was done and and 6 out of nine cases showed ositive test indicated by precipitation of proteins at 56-60 degree celcius and disappearance of turbidity at 100 degree celcius.

For confirmation of diagnosis, Serum Protein electrophoresis of these patients were done and were confirmed by presence of “M” band.

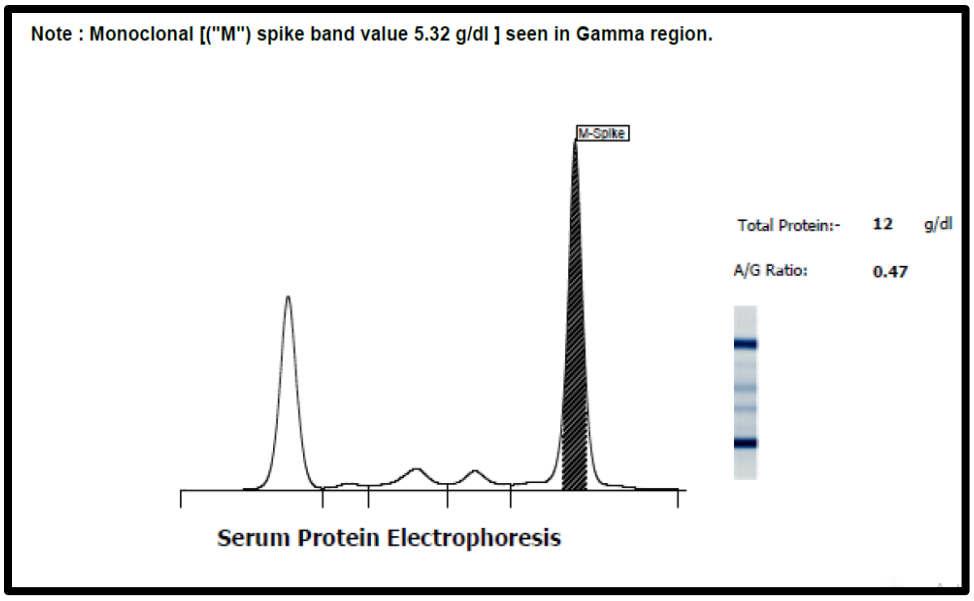


Figure 7: Monoclonal "M"spike seen in Serum Protein Electrophoresis.

DISCUSSION

Plasma cell Dyscrasias (PCD) are a group of varied heterogenous disorders which features expansion of clonal plasma cells thus producing ample quantities of monoclonal immunoglobulins [1]. In our retrospective study ranging over a san of three years; Nine cases of Multiple Myeloma/ Plasma Cell Myeloma were recovered and diagnosis was confirmed by serum electrophoresis.. The MM cases were diagnosed according to criterias given by International Myeloma working group criteria for classification of Monoclonal Gammopathies, MM and related disorders [1,2]. In the current study, all the cases occurred in older age group, and majority wre above 55 years of age. This finging is in concordance with the study done by C Fousad K et al, Kaustubh Bora et al, L A Jacob et al [1, 6-8]. The Plasma Cell Myeloma presents as a disease showing varied clinical spectrum ranging from asymptomatic disease to severe crippling disease, because of slow progression and affection of the bone marrow, skeletal system and proliferation of plasma cells. This is similar to findings of various national and international studies done by various authors [1,9,10]. Bone marrow findings of these lesion may show presence of plasmablastic cells along with mature lasma cells, thus making it exigent and highly challenging to correctly interpret the bone marrow aspiration findings. An unambiguous distinction is necessary between plasmablastic lymphoma and plasmablastic myeloma due to a great overlap in morphology, immunophenotypical features and clinical presentation; and a lack of definitive diagnostic criterias for the same [11].

CONCLUSION

To conclude, the treatment options for multiple myeloma have become more and more electrifying and exciting these days due to upcoming therapeutics techniques which are uniquely novel. Multiple new trials have grown roots and on their verge to establish their success stories in treating Mulyiple Myeloma [3].

This current study highlights the importance of Clinico-radio-pathological correlation in the diagnosis of these cases despite of the initial clinical diagnosis [11].

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