

Types of paraproteinemia in patients with multiple myeloma: A cross-sectional study

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Abstract

Objective: To determine the types of paraproteins in patients with multiple myeloma in a tertiary care setting.

Methods: The cross-sectional study was conducted at the Liaquat National Hospital, Karachi, from November 2015 to May 2016, and comprised patients with multiple myeloma selected using consecutive, non-probability sampling technique. Detailed history was taken and immunofixation assay was conducted to assess the type of paraproteins in the patients. Data was recorded on a proforma and analysed using SPSS 22.

Results: Of the 87 patients, 62(71.3%) were males and 25(28.7%) were females. The overall mean age was 57.41±10.53 years. Of the total, 52(71.3%), patients had Immunoglobulin G kappa and 61(70%) had Immunoglobulin A kappa paraprotein.

Conclusion: The most common types of paraprotein was found to be Immunoglobulin G kappa followed by Immunoglobulin A kappa.

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Introduction

Multiple myeloma (MM) is a malignancy of B-cell and is categorised by a monoclonal increment of plasma cells in the bone marrow.¹ Quarter of MM patients die within the 3 years of diagnosis and others carry the disease for more than 10 years.^{2,3} It accounts for 0.8% cases of cancer around the globe and holds 13% of haematological malignancies.^{3,4} MM is more prevalent in males compared to females with the ratio of 1.4:1.⁵ MM incidence increases progressively with age, percentage of cases occurring at age >50 years is 90% and average age at diagnosis is 70 years.¹

According to age, MM in African Americans is 2-fold higher (9.5 per 100,000 per year) compared to the whites (4.1 per 100,000 per year).¹

Monoclonal gammopathy of undetermined significance (MGUS) appears in 3% cases >50 years age.⁶ Most common clinical appearances include renal impairment, lytic bony lesions, anaemia, hypercalcaemia and immune dysfunction.^{1,7} Risk for growth of disease comprises gender, age, racial and cultural family background of MM and other lympho-haematopoietic cancers and some inherited factors.¹

In MM, each prolonged replica of malignant plasma cells form surplus of monoclonal protein (M-protein or paraprotein). Immunoglobulin (Ig) can be classified into

IgA, IgG, IgD, IgE and IgM based on the presence of distinct heavy chain polypeptide sequence.⁸ Apart from heavy chains, antibodies in MM are also classified as two distinct types of light chains as well, i.e. kappa and lambda.⁹ So, eventually myeloma can be classified by heavy and light chains such as IgG kappa, IgG lambda, IgA kappa or IgA lambda. Ig levels should be checked at the baseline and subsequently to monitor the response of the disease to therapy, conducting treatment and determining progression of the disease.

Data on MM from Pakistan is scarce. The current study was planned to assess the spectrum of paraproteinaemia in MM patients in the local population within a tertiary care setting.

Patients and Methods

The cross-sectional study was conducted at the Haematology Department of the Liaquat National Hospital (LNG), Karachi, from November 2015 to May 2016, and comprised patients of either gender age 40-80 years who had confirmed MM diagnosis and gave written informed consent. The patients were selected using consecutive non-probability sampling after approval from the institutional ethics review board as well as from the College of Physicians and Surgeons, Pakistan (CPSP).

The calculated sample size was n=85 patients, using openepi.com¹⁰ by anticipating 10% increase in immunoglobulin G frequency in multiple myeloma patients in previously published study¹¹ with 95% confidence level and 5% absolute precision.

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Demographic, clinical history and immunofixation result was recorded on a proforma for all the selected patients. Blood samples were taken for immunofixation assay, which was conducted through G-26 inter-lab automated instrument by gel electrophoresis method. Types of paraproteinaemia were labeled as IgG >16, IgA >4, kappa >13.5 and lambda >7.23, polyclonal gammopathy. Patients with MUGS or smouldering myeloma, amyloidosis and solitary plasmacytoma were excluded. Patients who received chemotherapy (treated) for MM or having a history of other malignancies were also excluded. In order to avoid confounding variables, the exclusion criteria was strictly applied.

Data was analysed using SPSS 22. Frequencies and percentages were calculated for quantitative variables and mean±standard deviation (SD) were calculated for numeric data. Chi-square test was applied to check the statistical significance at 0.05 α .

Results

Of the 87 patients, 62(71.3%) were males and 25(28.7%) were females. The overall mean age was 57.41±10.53 years. Of the total, 52(71.3%), patients had IgG kappa and 61(70%) had IgA kappa paraprotein. IgG lambda was found in 18(20.7%) and IgA lambda in 30(34.5%) patients (Table-1).

Overall, age was significantly associated with IgG kappa

Table-1: Frequency distribution of gender and stages of Multiple Myeloma.

Variable	Number (n)	Percentage (%)	
Gender			
Male	62	71.3	
Female	25	28.7	
Total	87	100	
Types of Paraproteinaemia	Yes	No	Total
IgG Kappa	62(71.3%)	25(28.7%)	87(100%)
IgG Lambda	18(20.7%)	69(79.3%)	87(100%)
IgA Kappa	61(70.0%)	26(29.9%)	87(100%)
IgA Lambda	30(34.5%)	57(65.5%)	87(100%)

Ig: Immunoglobulin.

($p=0.012$) and IgA kappa types ($p=0.019$) (Table-2). IgG types were predominantly associated with male gender (Table-3).

Discussion

In the current study the paraprotein types IgG kappa in 62 patients (71.3%), IgA kappa in 61 patients (70.0%) were the most frequent paraproteins, comparable to a literature showing 73% patients with IgG paraprotein, and 17.5% with IgA, while 70% were kappa chain-positive and 30% were lambda chain-positive.^{11,12} One study found monoclonal paraprotein in the blood serum of 22(88) patients, and paraprotein secretion was not present in three patients, along with noticed diminishing

Table-2: Types of paraproteinemia according to Age (n=87).

Age	Types of Paraproteinaemia							
	IgG Kappa		IgG Lambda		IgA Kappa		IgA Lambda	
	Yes	No	Yes	No	Yes	No	Yes	No
40-60 Years	49 (56.32%)	2 (2.29%)	16 (18.39%)	35 (40.22%)	50 (57.47%)	1 (1.14%)	11 (12.64%)	40 (45.97%)
61-80 Years	13 (14.94%)	23 (26.43%)	2 (2.29%)	34 (39.08%)	11 (12.64%)	25 (28.73%)	19 (21.83%)	17 (19.54%)
Total	62 (71.26%)	25 (28.73%)	18 (20.68%)	69 (79.31%)	61 (70.11%)	26 (29.88%)	30 (34.48%)	57 (65.51%)
	87 (100%)		87 (100%)		87 (100%)		87 (100%)	
P-value	0.012		0.993		0.019		0.846	

Ig: Immunoglobulin.

Table-3: Types of Paraproteinemia according to gender (n=87).

Gender	Types of Paraproteinemia							
	IgG Kappa		IgG Lambda		IgA Kappa		IgA Lambda	
	Yes	No	Yes	No	Yes	No	Yes	No
Male	55 (63.21)	7 (8.04%)	16 (18.3%)	46 (52.87%)	52 (59.77%)	10 (11.49%)	23 (26.43%)	39 (44.82%)
Female	7 (8.04%)	18 (20.6)	2 (2.29%)	23 (26.4%)	9 (10.34%)	16 (18.39%)	7 (8.04%)	18 (20.68%)
Total	62 (71.26%)	25 (28.73%)	18 (20.68%)	69 (79.31%)	61 (70.11%)	26 (29.88%)	30 (34.48%)	57 (65.51%)
	87 (100%)		87 (100%)		87 (100%)		87 (100%)	
P-value	0.000		0.053		0.000		0.291	

Ig: Immunoglobulin.

in gamma globulin levels and existence of plasma cells with abnormal immune phenotype in the bone marrow. Also, 14(63.6%) patients had IgG paraprotein, 8(36.4%) IgA.¹³ IgM monoclonal gammopathies presented greater mutational load as the disease grew, similar to up-ruling of pathogenic pathways.¹⁴

MM is a haematological malignancy usually presenting in the elderly, with a median age in India of 55-60 years. In the present study, the maximum number of cases were aged 40-60 years compared to one study showing five patients <60 years, whereas one was 37 years old, but the maximum number of cases were aged 60-70 years.¹⁵ It has been mentioned that approximately 2% MM patients are <40 years and it is still occasional in patients with age <30 years. In an Indian study, out of 150 MM cases reviewed over 10 years, 5(3.3%) were <30 years of age.¹⁵

A paraprotein, also called Bence Jones protein, is a monoclonal Ig light chain that is present in urine or blood rising from clonal expansion of mature B cells, plasma cells or B-lymphocytes. Other terms used are M-band or Monoclonal protein.¹⁶

In our study the average age was 57.41 ± 10.53 years while in individuals aged >50 years the occurrence of paraprotein was 3.2%; this differs from a previous study.¹⁷

IgG kappa, IgG lambda and IgA kappa types of paraproteinemia were common in those aged 40-60 years, while the only IgA lambda type of paraproteinemia was common in those aged 61-80 years. All types of paraproteinemia were predominant in the male gender. In one study,¹ all cases demonstrated monoclonal protein. On further categorisation, myeloma was IgG type in all cases, while in another study serum electrophoresis revealed M band in 82% patients. The band migrated in gamma range in 65.7%, in other ranges such as beta, alpha 2 and between gamma and beta, it was equally distributed, i.e., 5.7% each. M band was not seen in 17.1% patients.¹⁸ In our study, we did not find M band in other ranges.

A wide range of mature B cell dysfunction may be related to a circulating paraprotein. After reviewing 1000 cases of M protein, a study observed at the Mayo clinic the diagnosis was MM in 18% cases.¹⁹

It is crucial that blood and urine may be screened for paraprotein if taking myeloma as a diagnosis as 15% cases of Myeloma monoclonal Ig light chain may be the lone M-protein present. Such type of cases may be overlooked if serum protein electrophoresis was only performed in query. In clinical practice, the measurement

of serum-free light chain is recently introduced which can permit the quantification of free kappa and lambda light chains divided by plasma cells. An abnormal standard kappa-lambda average shows an augmentation of one light chain type, though the mechanism is not clearly stated, is applied as replacement indicator for clonal growth. The usage of serum exam will repeal the necessity to test urine and blood so that the diagnosis can be conducted.²⁰

As for the prognosis, the value is added by the few risk factors that are related with M protein level, MGUS type, and free light-chain ratio of serum. It has been suggested that the conquest of uninvolved Igs, particularly Ig of the same type, may be related to the increased progression risk.^{21,22}

In a study in Sweden, 728 patients were investigated with MGUS, and it was indicated that the dominance of one or two Igs was related to the increased progression risk compared to those who were without suppression of one or two Igs, whereas the overall development risk in the investigation was computed to be 0.5% per year.²²

In terms of limitations, the current study had a small sample size. Studies with larger sample sizes are required using standard measurement approaches. Besides different haematologists were involved in the current study.

Conclusion

Detection of the type of monoclonal component in the blood is important for MM diagnosis and monitoring. The most common types of paraprotein in MM patients in the study were IgG kappa and IgA kappa.

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Conflict of Interest: None.

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