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Research Article

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Evaluation of M-Protein Patterns and Different Correlations in Patients with Multiple Myeloma

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Abstract

Introduction: *M-protein plays an important role in diagnosis, prognosis and treatment monitoring in Multiple Myeloma.*

Aim of the study: *This study aimed to evaluate M-protein patterns and their different correlation in patients with Multiple Myeloma.*

Methods: *This descriptive cross-sectional study was conducted in the Department of Hematology at Shaheed Ziaur Rahman Medical College Hospital and private consultation center in Bogura from 2019 to 2024. A total of 77 confirmed multiple myeloma patients were included. M-protein was analyzed using serum protein electrophoresis, immunofixation and immunoturbidimetry alongside routine biochemical parameters. Data were statistically analyzed using SPSS version 25.0. Ethical approval was obtained from the institutional review board. Results: A total of 77 patients with multiple myeloma were analyzed. Most participants were aged >50 years (83.1%), with a male predominance (64.9%). The gamma region was the most frequent M-protein electrophoretic zone (72.7%), followed by the beta-2 region (26.0%). IgG was the predominant heavy chain (57.1%), while kappa light chains were more common than lambda (64.9% vs. 35.1%). Combined heavy- and light-chain expression was observed in 87.0% of cases, and the most frequent subtype was IgG–kappa (36.4%). The mean M-protein concentration was 3.38 ± 2.28 g/dL; 45.5% had levels >3 g/dL, and 33.8% showed an involved/uninvolved light chain ratio >100, with both criteria present in 13.0%. Elevated M-protein (>3 g/dL) was significantly associated with heavy chain type ($p = 0.036$) but not with light chain type ($p = 0.896$). Quantitative M-protein correlated strongly with total serum protein ($r = 0.937$, $p < 0.001$) and inversely with serum albumin ($r = –0.344$, $p = 0.002$) and albumin–globulin ratio ($r = –0.792$, $p < 0.001$). A significant association was*

observed between heavy chain type and electrophoretic zone ($p < 0.001$), with IgG predominating in the gamma region and IgA in the beta-2 region.

Conclusion: *This study shows that M-protein patterns in Bangladeshi multiple myeloma patients commonly exhibit IgG–kappa predominance and gamma-region migration. Quantitative M-protein levels correlate strongly with total serum protein and inversely with serum albumin and albumin–globulin ratio, reflecting the disease's biology. Only a small number of patients met both M-protein >3 g/dL and light chain ratio >100, indicating significant biological variability. The relationship between heavy chain subtype and migration zone, along with IgG subtype and higher M-protein concentration, highlights the importance of combined electrophoretic and immunoglobulin profiling in diagnostics.*

Keywords: Multiple-Myeloma, M-protein, Electrophoresis

1. Introduction

Multiple myeloma is a form of cancer that originates in a type of white blood cell known as a plasma cell. Normal plasma cells aid the immune system by producing proteins called antibodies. Antibodies detect and target germs. In multiple myeloma, cancerous plasma cells accumulate in the bone marrow [1]. A group of plasma cells began to multiply uncontrollably and produce a large number of single abnormal antibodies instead of producing many useful antibodies. This abnormal protein, called monoclonal protein or M-protein, plays a key role to detect and monitor diseases [2,3]. M protein is usually present in blood or urine and can be detected by tests such as serum protein electrophoresis and immune mixing [4]. These tests are widely used because they are relatively cheap and available in many hospitals. Although the M-protein may look just like a strip in a laboratory report, it actually carries valuable information about the nature, severity, and progression of the disease [5]. The type of M protein, whether IgG, IgA, or just a light chain such as kappa or lambda, can provide insight into how the disease may manifest and what complications may develop [6]. Certain types of M protein are associated with more aggressive forms of disease or specific problems such as kidney or bone damage. For example, light chain myeloma tends to affect the kidneys more severely, while IgA myeloma can progress faster than other types [7]. Understanding these patterns is important not only for scientific research but can also have a direct impact on patient care, helping doctors predict complications and plan treatment more effectively. Many other studies have reported that patients with multiple myeloma are usually diagnosed at a late stage. This is partly due to a lack of awareness and limited access to advanced diagnostic tools [8,9]. However, if interpreted correctly, basic laboratory tests for the detection and quantification of M-protein can still provide valuable information. Unfortunately, there is very little local data on how various M-protein structures manifest themselves in our population or how they relate to common clinical manifestations such as anemia, bone pain, calcium levels, and kidney function [10]. By studying these relationships in more detail, we will be able to gain a clearer understanding of how multiple myeloma behaves in our medical environment. This can help doctors identify patterns at an earlier stage, deal more actively with complications, and may improve treatment outcomes for patients with this complex disease [11]. It also allows us to compare the results of our studies with international ones and find out whether certain patterns are more common or more severe in our patient population. The purpose of this study was to evaluate the pattern and different aspect of M-protein in patients with multiple myeloma and its relationship with demographic and laboratory parameters.

2. Methods

This descriptive cross-sectional study was conducted in the Department of Hematology at Shaheed Ziaur Rahman Medical College Hospital and private consultation center in Bogura, over a five-year period from 2019 to 2024. A total of 77 patients diagnosed with multiple myeloma were enrolled. Data were collected from clinical records, laboratory reports, and direct patient interviews using a structured data sheet. M-protein was detected and characterized using serum protein electrophoresis, immunofixation and immunoturbidimetry techniques. Additional biochemical parameters such as total protein, serum albumin, albumin-to-globulin ratio, and light chain ratios were measured using standard laboratory procedures. Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 25.0. Descriptive statistics were used to summarize the data, while Pearson correlation coefficients were applied to examine associations between variables. Ethical approval for the study was obtained from the Institutional Review Board of Shaheed Ziaur Rahman Medical College, and informed consent was obtained from all participants.

Inclusion criteria

- Patients with a confirmed diagnosis of multiple myeloma based on clinical and laboratory findings.

Exclusion criteria:

- Patients with smoldering multiple myeloma or any diagnostic dilemma.
- Patients who did not provide consent to participate in the study

3. Results

Variable	Category	Frequency (n)	Percentage (%)
Age Group	<30 years	1	1.3
	30–50 years	12	15.6
	>50 years	64	83.1
Gender	Male	50	64.9
	Female	27	35.1

Table 1: Baseline Demographic Characteristics of the Study Population (n = 77)

A total of 77 patients diagnosed with multiple myeloma were included in the study. The majority of the participants (83.1%) were over 50 years of age, while 15.6% were between 30–50 years and only 1.3% were below 30 Years. Males constituted 64.9% (n = 50) of the cohort and females accounted for 35.1% (n = 27).

Variable	Category	Frequency (n)	Percentage (%)
M-Protein Zone	Gamma	56	72.7
	Beta-2	20	26.0
	Beta-1	1	1.3
Electrophoretic 2nd Peak	No 2nd peak	62	80.5
	gamma region	10	13.0
	beta-2 region	4	5.2
	beta-1 region	1	1.3

Table 2: Distribution of M-Protein Zone and Electrophoretic Peak Pattern

Among the patients, the most common zone of M-protein was the gamma region (72.7%), followed by beta-2 (26.0%), and beta-1 (1.3%). Regarding the electrophoretic 2nd peak pattern (in association with top peak), 80.5% showed no secondary peak, while 13.0% had a significant secondary peak in gamma region, 5.2% in beta2 region and 1.3% in beta1 region.

Chain Type	Category	Frequency (n)	Percentage (%)
Heavy Chain	IgG	44	57.1
	IgA	18	23.4
	IgM	6	7.8
	Not detected	9	11.7
Light Chain	Kappa	50	64.9
	Lambda	27	35.1

Table 3: Heavy and Light Chain Distribution Among MM Patients

IgG was the most frequently detected heavy chain (57.1%), followed by IgA (23.4%) and IgM (7.8%). In 11.7% of patients, no heavy chain was detected. Among light chains, kappa was predominant (64.9%) and lambda accounting for 35.1%.

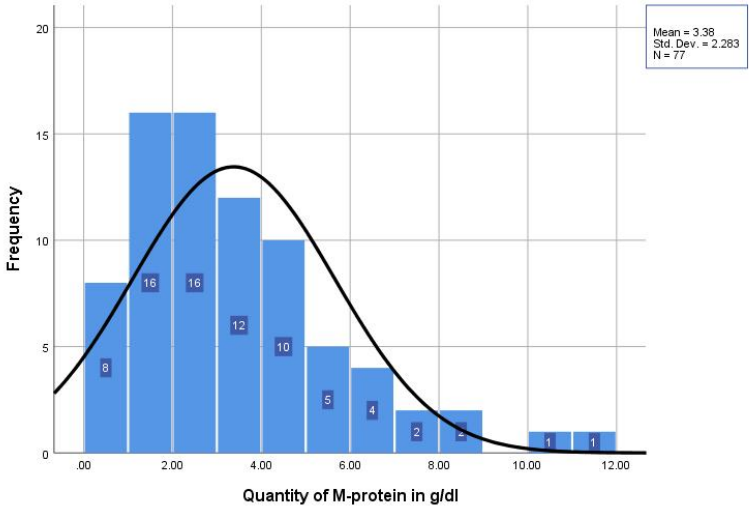

Figure 1: Histogram Showing Distribution of Quantitative M-Protein Levels

Figure 1 shows the distribution of M-protein levels in 77 multiple myeloma patients. Most values ranged between 2–5 g/dL, with a mean of 3.38 ± 2.28 g/dL. The data show a right-skewed pattern, indicating variability in M-protein concentrations across patients.

Pattern of Expression	Frequency	Percentage
Light chain only	8	10.4
Heavy chain only	2	2.6
Both heavy and light chains	67	87.0
Most common subtype		
IgG–Kappa	28	36.4

Table 4: Immunoglobulin Chain Expression Pattern (n = 77)

This table describes patterns of immunoglobulin secretion. Combined heavy- and light-chain expression was observed in 67 patients (87.0%), while light-chain–only disease accounted for 10.4% (8/77) and heavy-chain–only expression for 2.6% (2/77). The most common subtype was IgG–kappa (28/77, 36.4%).

Parameter	Frequency (n)	Percentage (%)
Mean M-protein level (g/dL), Mean ± SD	3.38 ± 2.28	
Mean Light Chain Ratio (LCR), Mean ± SD	79.35 ± 249.80	
M-protein >3 g/dL	35	45.5
M-protein <3 g/dL	42	54.5
Involved/Uninvolved light chain ratio >100	26	33.8
Involved/Uninvolved light chain ratio <100	51	66.2
Both criteria met (M-protein >3 g/dL and ratio >100)	10	13.0

Table 5: Quantitative M-Protein and Light Chain Ratio Profile (n = 77)

In this table, the mean M-protein level was 3.38 ± 2.28 g/dL, and the mean Light Chain Ratio (LCR) was79.35 ± 249.80. Elevated M-protein levels (>3 g/dL) were found in 35 patients (45.5%), while 33.8% (26/77) had an involved/uninvolved light chain ratio >100. Both criteria were met in 10 patients (13.0%).

Variable	Category	χ^2 (Chi-square)	df	p-value
Heavy Chain Type × M-Protein (>3 g/dL)	IgG, IgA, IgM	8.525	3	0.036
Light Chain Type × M-Protein (>3 g/dL)	Kappa, Lambda	0.017	1	0.896

Table 6: Association Between M-Protein Concentration (>3 g/dL) and Chain Type (n = 77)

A significant association between heavy chain type and elevated M-protein levels (>3 g/dL) ($\chi^2 = 8.525$, df = 3, p = 0.036). Patients with IgG heavy chains were more likely to have M-protein levels above 3 g/dL. However, there was no significant association between light chain type (κ vs λ) and M-protein levels ($\chi^2 = 0.017$, df = 1, p = 0.896).

Variable	r-value (qMpro)	p-value	Significance
Light Chain Ratio (LCR)	–0.113	0.328	NS
Total Protein (TP)	0.937	<0.001	Significant
Serum Albumin	–0.344	0.002	Significant
Albumin: Globulin Ratio	–0.792	<0.001	Significant

Table 7: Pearson Correlation Between Quantitative M-Protein and Biochemical Parameters (n = 77)

Pearson correlation analysis revealed a strong positive correlation between quantitative M-protein and total serum protein (r = 0.937, p < 0.001). In contrast, serum albumin and AGR showed significant negative correlations with qM-protein (r = –0.344 and –0.792, respectively; both p < 0.01). The light chain ratio had no significant correlation with M-protein levels (p = 0.328).

M-Protein Zone	IgG n (%)	IgM n (%)	IgA n (%)	None n (%)	Total n (%)
Gamma	42 (75.0)	3 (5.4)	3 (5.4)	8 (14.3)	56 (72.7)
Beta-2	2 (10.0)	3 (15.0)	14 (70.0)	1 (5.0)	20 (26.0)
Beta-1	0 (0.0)	0 (0.0)	1 (100.0)	0 (0.0)	1 (1.3)
Total	44 (57.1)	6 (7.8)	18 (23.4)	9 (11.7)	77 (100)
*Statistical test: Pearson $\chi^2 = 43.406$, df = 6, p < 0.001.					

Table 8: Relationship Between Heavy Chain Type and M-Protein Electrophoresis Zone (n = 77)

The relationship between heavy chain type and M-protein electrophoretic zone. The gamma region was predominantly associated with IgG heavy chains (75.0%), whereas the beta-2 region was mainly associated with IgA (70.0%). A statistically significant association was observed between heavy chain type and M-protein zone ($\chi^2 = 43.406$, df = 6, p < 0.001).

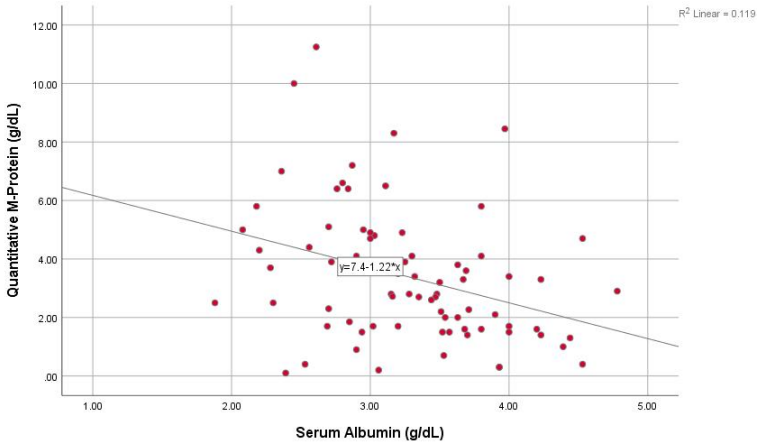

Figure 2: Scatter Plot of qM-Protein vs Serum Albumin

Figure 3 shows a scatter plot illustrating the inverse relationship between M-protein quantity and serum albumin levels. As albumin decreases, M-protein tends to increase. The linear trendline ($y = 7.4 – 1.22*x$) suggests a weak negative correlation ($R^2 = 0.119$), indicating some variability but a general trend.

4. Discussion

This study provided insight into the biochemical and electrophoretic characteristics of M-protein in Bangladeshi patients with multiple myeloma (MM). Our demographic profile showed 83.1% of patients over 50 years and 64.9% male predominance, closely mirroring global epidemiological data. Samba et al. reported a similar age distribution in West Africa (mean age 59.6 years), while Mohammed et al. found a 68% male predominance in India, suggesting consistent demographic patterns across developing regions (12, 13). All 77 patients (100%) demonstrated detectable M-protein, with gamma region predominance (72.7%) being the most common location. This aligns with Samba et al., who reported 76.7% gamma region M-protein in their Senegalese cohort (13). However, our beta-2 region involvement (26%) was notably higher than their 23.3%, potentially reflecting regional variation or methodological differences in electrophoresis interpretation. The single beta-1 case (1.3%) was comparable to international frequencies. The heavy and light chain distribution IgG (57.1%), IgA (24.7%), light chain only (18.2%) closely matched global patterns. Samba et al. reported IgG 60%, IgA 23.3%, and light chain 16.7%, demonstrating remarkable consistency [14]. Similarly, our kappa predominance (64.9%) over lambda (35.1%) maintained the expected 2:1 physiological ratio observed worldwide. Mohammed et al. found similar kappa dominance (65%) in their Indian series, suggesting stable immunoglobulin genetics across South Asian populations [12]. A critical finding was that only 13% (10/77) of confirmed MM patients fulfilled both traditional diagnostic thresholds simultaneously (M-protein >3 g/dL AND involved/uninvolved light chain ratio >100). This contrasts sharply with diagnostic expectations and raises important questions about threshold applicability in our population. When analyzed separately, 54.5% had M-protein >3 g/dL, while a different subset exceeded light chain ratio >100. Fernandez de Larrea et al. demonstrated similar heterogeneity in smoldering myeloma, showing substantial M-protein evolution variability with some patients progressing despite modest levels [14]. Silva et al. emphasized that light chain-only myeloma frequently presents diagnostic challenges precisely because conventional M-protein thresholds may not be met despite clinically significant disease [15]. Patients with M-protein >3 g/dL showed significant association with IgG heavy chain type ($p = 0.036$), suggesting intact immunoglobulin-producing clones generate higher absolute M-protein quantities. Wijnands et al. confirmed this using mass spectrometry, demonstrating that intact IgG-based M-protein is typically more abundant and readily detectable than free light chains [16]. Our mean M-protein level (3.38 ± 2.28 g/dL) closely approximated Mohammed et al.'s Indian cohort (3.61 ± 2.1 g/dL), indicating comparable disease burden at presentation across South Asia [12]. Patients with intact immunoglobulin (IgG/IgA) exhibited higher M-protein levels (~3.78 g/dL) versus light chain-only disease (0.93 g/dL), consistent with Wijnands' findings. The light chain ratio (mean 79.35 ± 249.80) showed considerable variability but did not significantly correlate with absolute M-protein levels. This apparent discordance differs from Askari et al., who emphasized that highly skewed ratios (>100 or <0.01) correlated with aggressive disease and early progression in light chain myeloma [17]. However, Askari's work focused primarily on light chain disease, whereas our cohort was predominantly IgG/IgA myeloma. In intact immunoglobulin disease, light chains remain bound within antibody structures rather than circulating freely, explaining less dramatic ratio elevations despite high total M-protein. This mechanistic distinction is critical for interpreting subgroup differences. In this study, electrophoretic migration patterns demonstrated a strong association between heavy chain subtype and M-protein localization ($\chi^2 = 43.406$, $p < 0.001$). IgG paraproteins predominantly migrated in the gamma region, whereas IgA paraproteins showed a marked tendency toward beta-2 region migration. This pattern reflects known physicochemical properties of IgA molecules, including polymerization and altered charge, and has been consistently reported in a study by Jia et al. (2025) [18]. The frequency of secondary or double M-protein peaks in this study, 19.5% incidence of double peaks (secondary M-protein spikes) exceeded typical international reports. Importantly, patients with single peaks demonstrated higher average M-protein levels than those with double spikes, suggesting the second peak may represent either biclonal disease, oligoclonal reconstitution, or residual polyclonal production rather than additional tumor burden. Dash and Mohanty reported similar phenomena, cautioning that secondary peaks could complicate diagnosis if not properly characterized by immunofixation [18]. Some secondary peaks may represent co-existing MGUS clones rather than dual malignant populations. Biochemical correlations strongly validated established pathophysiology. The robust positive correlation between total protein and M-protein ($r = 0.937$, $p < 0.001$) confirmed M-protein as the primary driver of hyperproteinemia. Inverse correlations with albumin ($r = -0.344$, $p = 0.002$) and albumin:globulin ratio ($r = -0.792$, $p < 0.001$) reflected suppressed hepatic albumin synthesis during myeloma progression. Mohammed et al. documented this pattern across ISS stages, with stage III patients showing lowest albumin (3.05 g/dL) and highest M-protein (3.61 g/dL), consistent with our inverse relationship ($R^2 = 0.119$) [12]. The revised ISS staging incorporates low albumin (<3.5 g/dL) as adverse prognostic marker, validating clinical relevance [1]. Our findings must be interpreted considering methodological limitations. Conventional serum protein electrophoresis, while appropriate for resource-limited settings, has lower sensitivity than mass spectrometry approaches. Wijnands et al. demonstrated that ultra-sensitive targeted mass spectrometry detects minimal residual disease with superior precision, potentially explaining light chain ratio correlation variability [19]. The cross-sectional design precluded longitudinal M-protein evolution assessment. MM patients showed M-protein patterns largely consistent with international data particularly heavy chain distribution, kappa:lambda ratios, and biochemical correlations, important differences emerged. The low proportion (13%) meeting both quantitative thresholds simultaneously, higher secondary peak frequency, and subgroup heterogeneity when stratifying by M-protein levels (>3 vs <3 g/dL) and light chain ratios (>100 vs <100) highlight the need for nuanced diagnostic approaches. The significant IgG association with higher M-protein levels and robust biochemical correlations underscore

that integrating multiple parameters provides superior diagnostic and prognostic information compared to single thresholds. These findings emphasize that even in resource-limited settings, careful electrophoresis interpretation alongside routine blood tests can guide clinical management effectively while acknowledging regional variations in disease presentation.

5. Conclusion

This study demonstrates that the electrophoretic and immunochemical patterns of M-protein in Bangladeshi patients with multiple myeloma, with IgG–kappa predominance and gamma-region migration being most common. Quantitative M-protein levels showed strong positive correlation with total serum protein and significant inverse correlations with serum albumin and albumin–globulin ratio, reflecting established disease biology. Importantly, only a small proportion of patients simultaneously fulfilled both conventional diagnostic thresholds of M-protein >3 g/dL and an involved/uninvolved light chain ratio >100, highlighting substantial biological heterogeneity and potential limitations of relying on single quantitative cut-offs. The significant association between heavy chain subtype and electrophoretic migration zone, as well as between IgG subtype and higher M-protein concentration, underscores the diagnostic value of integrated electrophoretic and immunoglobulin profiling.

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