Original Article

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The Pattern of Immunoglobulin Production in Secretory Myeloma and the Relationship Between Relevant Hematological and Clinical Parameters in Basrah

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ABSTRACT

Background: Plasma cell disorders encompass a spectrum of diseases ranging from benign to malignant. Among malignant plasma cell disorders, multiple myeloma is the most common and well-recognized entity. **Aim**: To identify the pattern of immunoglobulin production in secretory myeloma in Basra and correlate findings with hematological and clinical data. **Methods**: A retrospective study of 143 patients with plasma cell disorders was conducted at the Department of Pathology, Basrah Oncology Center, Iraq. Clinical data, relevant laboratory parameters (erythrocyte sedimentation rate, renal function tests, and serum calcium), bone marrow examination findings, radiological findings of bony lesions, and results from serum/urine protein electrophoresis and immunofixation or flow cytometric immunophenotyping were analyzed in conjunction with medical records. **Results**: Abnormal urine protein electrophoresis was found in 93.4% of patients, with most M bands located in the gamma region. The most prevalent subtype was IgG kappa, accounting for 68% of cases. This was followed by IgG lambda (17%), IgM lambda (6.5%), IgM kappa (3.2%), IgA kappa (1.3%), and free light chains (1.3%). Laboratory parameters showed wide variability, with a median hemoglobin of 9.1 g/dL, serum calcium of 9.9 mg/dL, and erythrocyte sedimentation rate of 80 mm/hr. Significant associations were found between immunofixation electrophoresis subtypes and erythrocyte sedimentation rate, serum calcium, and urea. Notably, the IgA kappa group had higher serum calcium (mean 12.45 mg/dL, $p = 0.020$). Radiological findings revealed multiple bony lesions in the majority of patients. **Conclusions**: Serum protein electrophoresis is a useful initial screening tool for detecting paraproteinemia, but it lacks sensitivity for accurately characterizing monoclonal proteins. Immunofixation, by contrast, provides higher sensitivity and allows precise identification of monoclonal immunoglobulin subtypes. In our cohort, IgG kappa was the predominant subtype, aligning with global trends, whereas patients with the IgA isotype exhibited more severe laboratory abnormalities.

Keywords: Plasma cell disorders, Multiple myeloma, Serum protein electrophoresis.

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INTRODUCTION

Plasma cell neoplasms (PCNs) are a group of mature B-cell disorders characterized by the clonal proliferation of plasma cells that secrete monoclonal immunoglobulins, commonly referred to as paraproteins or M-proteins.[1] Plasma cell disorders (PCDs) are classified into premalignant conditions such as monoclonal

gammopathy of undetermined significance and smoldering multiple myeloma, and malignant disorders including multiple myeloma, plasma cell leukemia, and extramedullary plasmacytoma. Other related entities include solitary plasmacytoma of bone, Waldenström macroglobulinemia, AL amyloidosis, and POEMS syndrome. The classification reflects a progression from asymptomatic precursor states to overt malignancy with end-organ damage.[2] Multiple myeloma (MM) is a malignant plasma cell disorder characterized by clonal proliferation in the bone marrow and secretion of monoclonal immunoglobulins (M protein) in serum and/or urine (secretory myeloma). Cases lacking detectable M protein by immunofixation are termed non-secretory MM (NSMM), initially reported in 3–5% of patients. With the introduction of high-sensitivity serum-free light chain (SFLC) assays, most of these NSMMs are now recognized as oligo-secretory forms. MM remains incurable, though modern combination therapies have improved survival.[3] The exact etiology is unclear, but recurrent mutations and translocations, particularly involving chromosome 14, are frequent. Monoclonal gammopathy of undetermined significance (MGUS) represents an early stage, progressing to MM or related disorders at a rate of 1% per year.[4] Clinical features in MM include bone lesions, hypercalcemia, abnormal paraproteins, immunodeficiency, anemia, renal failure, and amyloidosis. Prognostic factors include patient characteristics such as age and performance status, tumor burden including anemia, renal impairment, and elevated β2-microglobulin, plasma cell features such as proliferation rate and cytogenetic abnormalities like t(4;14) and t(14;16), and, most importantly, response to treatment.[5] Bone marrow aspiration (BMA) is essential for assessing marrow cellularity and morphology, while bone marrow biopsy (BMB) provides architectural and prognostic information.[6,7] Serum protein electrophoresis (SPE) separates serum proteins into albumin and globulin fractions. Albumin, the largest and most abundant protein, produces the tallest peak and migrates closest to the positive electrode, while globulins (α1, α2, β1, β2, and γ) migrate toward the negative pole, with the γ region furthest. In MM, a sharp γ-region peak (M spike) is typical. SPE is widely used as an initial test to detect monoclonal gammopathy and estimate M protein levels. Immunophenotyping by flow cytometry (FCM) is integral to the management of multiple myeloma. It enables accurate diagnosis through the distinction between clonal abnormal and normal plasma cells and assists in disease classification by differentiating multiple myeloma from precursor states such as MGUS and smoldering myeloma. Prognostically, a higher proportion of normal plasma cells at diagnosis is associated with lower disease burden and improved survival outcomes. Additionally, flow cytometry provides a highly sensitive tool for monitoring, particularly in the detection of minimal residual disease, and the characterization of antigen expression profiles offers insights that may inform therapeutic decision-making.[8] This study aims to identify the pattern of immunoglobulin production in secretory myeloma patients in Basra and to examine the relationship between these findings and important hematological and clinical parameters

MATERIALS AND METHODS

This retrospective study was conducted at the Department of Pathology, Basrah Oncology Center, Iraq, involving 143 patients diagnosed with plasma cell disorders who were referred for SPE and immunofixation electrophoresis (IFE) or for flow cytometric immunophenotyping of plasma cells between October 2022 and October 2024. Patient demographic and clinical data were obtained through medical record review. Laboratory records from the past two years, including SPE, urine protein electrophoresis (UPE), and IFE or immunophenotyping, were analyzed and correlated with the patients' clinical features. SPE was performed using capillary electrophoresis, which separates serum proteins into five distinct zones: albumin, alpha-1 globulins (such as alpha-1-antitrypsin), alpha-2 globulins (including haptoglobin and ceruloplasmin), β-globulins (including transferrin and β-lipoprotein), and γ-globulins (such as immunoglobulins IgG, IgA, and IgM). IFE was performed to confirm and characterize monoclonal proteins by immunoprecipitation with specific antisera against heavy chains (IgG, IgA, IgM) and light chains (kappa, lambda). Relevant laboratory parameters, including erythrocyte sedimentation rate (ESR), renal function tests, and serum calcium levels, were collected from patient records and the laboratory database. Bone marrow examination results, reported by hematopathologists, were also reviewed. SPE and immunotyping procedures were carried out using the Sebia Minicap Flex Piercing capillary electrophoresis system. The diagnosis of MM and PCDs was established according to the International Myeloma Working Group (IMWG) criteria., which require ≥10% clonal plasma cells in the bone marrow or biopsy-proven plasmacytoma,

together with one or more myeloma-defining events (such as hypercalcemia, renal impairment, anemia, or lytic bone lesions, or biomarkers of malignancy including clonal bone marrow plasma cells ≥60%, an involved/uninvolved serum free light chain ratio ≥100, or >1 focal lesion on MRI). Patients with plasma cell disorders not meeting the full criteria for MM, such as MGUS and smoldering myeloma, were diagnosed based on standard WHO/IMWG guidelines. Cases with incomplete reports, missing essential laboratory data, or insufficient clinical information were excluded at the outset; thus, only patients with complete datasets were included in the final analysis. Ethical approval was obtained from the scientific and ethical committees of both the Iraqi Board for Medical Specializations and the Basrah Health Directorate prior to data collection. Statistical analyses were carried out using the Statistical Package for the Social Sciences (SPSS), version 22. Categorical data were analyzed using descriptive statistics, including frequency distributions and percentage values. Continuous data were expressed as means, standard deviations, and ranges to illustrate their central tendency and dispersion. To compare numerical variables across multiple groups, a One-Way Analysis of Variance (ANOVA) was employed. A p-value of less than 0.05 was considered to denote statistical significance.

RESULTS

The demographic analysis (Table 1) highlights that the study included 143 patients with a mean age of 63.43 years (range: 28 to 88 years). Males constituted 64.3% of the participants, while females made up 35.7%.

Imaging findings (Figure 1) reveal that numerous bony lesions were the most frequent abnormality, observed in 70.59% of patients, followed by solitary bony lesions in 9.15%. Just 20.26% of the imaging findings were within normal limits.

Laboratory results (Table 2) show significant variability among the parameters. For example, the median serum calcium (S. Ca) was 9.90 mg/dL (range: 7.10–15.00 mg/dL), the median hemoglobin (Hb)Hb was 9.10 g/dL (range: 5.40–13.00 g/dL), and the median erythrocyte sedimentation rate (ESR) was 80 mm/hr. (range: 20–140 mm/hr.). SPE findings (Table 3) reveal that abnormal serum protein electrophoresis (SPE) was found in 96.5% of patients.

The analysis of M-protein spike characteristics (Table 4) shows a median level of 3.11 g/dL (range: 1.0–6.0 g/dL), with 83.2% of peaks located in the gamma region. Peaks in other regions, such as the beta (9.1%) and alpha regions (1.4%1.4%%), were less common.

Immunoglobulin subtype analysis (Table 5) indicates that IgG kappa was the most prevalent subtype, observed in 71.3%% of patients, followed by IgG lambda (17.5%%). Other subtypes, including IgM lambda(4.9%%),IgM kappa (3.5%), and IgA kappa (1.4%), were much less frequent.

Associations between immunoglobulin subtypes and laboratory parameters (Table 6) reveal significant findings between immunofixation electrophoresis subtypes and each of ESR, serum calcium, and Urea level. Notably, the IgA kappa group exhibited increased serum calcium levels (mean: 12.45 mg/dL, p = 0.020) compared to other subtypes. Hemoglobin levels varied among subtypes but did not reach statistical significance (p = 0.264).

Table 1: Demographical data of the studied patients

Variable		Count	Percentage %
Sex N= 143	Male	92	64.3%
	Female	51	35.7%
Variable		Mean ± SD	Range
Age (years)		63.43 ± 25.7	28 - 88

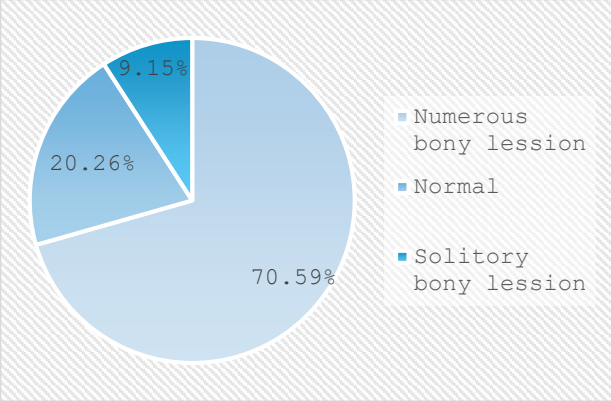

Figure 1: Pie chart of imaging findings of the patients.

Table 2: Laboratory results among enrolled patients

Variable	Median	Range	Minimum	Maximum
S. Ca (mg/dL)	9.90	7.10	7.90	15.00
HB (g/dL)	9.10	7.60	5.40	13.00
WBC (×10³/µL)	6.50	19.35	1.35	20.70
Platelet (×10³/µL)	181.00	449	63	512
Albumin (g/L)	44.40	52.00	18.90	70.90
Urea (mg/dL)	44.00	116.80	15.20	132.00
Creatinine (mg/dL)	0.90	12.47	0.43	12.90
ESR (mm/hr)	80.00	120	20	140

Table 3: SPE results among the patients

Variables		Frequency	Percentage %
SPE Type	Normal	5	3.5%
	Abnormal	138	96.5%
Total		143	100.0%

Table 4: M-Protein spike characteristics

Statistic	M-Protein (g/dL)
Median (g/dL)	3.11 ± 0.48
Range (g/dL)	5.0
Minimum (g/dL)	1.0
Maximum (g/dL)	6.0
M-protein Spike	Concentration (number of patients with M- spike) (%)
Peak within the Gamma region	119 (83.2%)
Peak within the Beta region	13 (9.1%)
Peak at Beta-Gamma junction	4 (2.8%)
Peak within the Alpha region	2 (1.4%)
Normal	5 (3.5%)

Table 5: Types of immunoglobulins among the patients

Frequency	count	(%)
IgG kappa / Restricted	102	71.3
IgG lambda / Restricted	25	17.5
IgM kappa / Restricted	5	3.5
IgM lambda / Restricted	7	4.9
IgA kappa / Restricted	2	1.4
Others	2	1.4
Total	143	100.0

Table 6: The association between immunofixation electrophoresis subtypes and laboratory parameters

IFE Group	N	Laboratory parameters (Mean ± SD)							
		ESR (mm/hr)	S. Ca (mg/dL)	Urea (mg/dL)	Albumin (g/L)	Platelet (×10³/µL)	WBC (×10³/µL)	Creatinine (mg/dL)	Hb (g/dL)
IgA Kappa	2	78.00 ± 15.00	12.45 ± 0.92	45.20 ± 9.00	38.20 ± 1.00	108.00 ± 5.66	4.25 ± 2.76	1.23 ± 0.43	6.50 ± 1.56
IgG Kappa	102	79.41 ± 25.77	10.32 ± 1.31	43.11 ± 16.72	45.09 ± 13.03	187.45 ± 79.55	7.16 ± 3.28	1.38 ± 1.03	9.38 ± 1.81
IgG Lambda	25	80.50 ± 33.40	10.07 ± 1.23	45.29 ± 30.04	44.45 ± 14.95	194.65 ± 88.49	6.65 ± 2.44	2.08 ± 3.40	9.54 ± 1.37
IgM Kappa	5	97.75 ± 0.50	9.28 ± 0.77	64.68 ± 2.65	35.22 ± 5.17	169.40 ± 49.89	6.94 ± 1.33	2.90 ± 0.61	10.04 ± 1.03
IgM Lambda	7	74.30 ± 35.27	9.62 ± 0.53	37.89 ± 10.24	51.60 ± 8.29	261.30 ± 159.72	7.78 ± 2.05	0.74 ± 0.16	9.14 ± 2.17
Others	2	92.33 ± 4.04	10.88 ± 1.68	68.23 ± 6.52	38.33 ± 16.33	164.83 ± 53.03	7.88 ± 3.96	2.73 ± 0.64	9.52 ± 1.87
P-Value		0.001	0.027	0.006	0.067	0.254	0.613	0.52	0.079

Table 7 shows the relationship between SPE and IFE results. The peak within the gamma region by SPE showed mostly IgG/kappa restricted (74.8%) by IFE, followed by IgG/lambda restricted (18.5%) and IgM/lambda restricted (3.3%). The peak within the beta region by SPE showed mostly IgG/kappa restricted (38.5%). The peak at the beta-gamma junction showed an equal number of IgG/kappa restricted and IgM/lambda restricted patterns. Normal SPE showed IgG/kappa restricted (80%) and IgM/lambda restricted (20%) by IFE

Table 7: The association between SPE and IFE results

SPE Result	IFE Subtype	Number (%)
Peak within the Gamma region (119)	IgG/ kappa restricted	89 (74.8)
	IgG/ lambda restricted	22 (18.5)
	IgM/lambda restricted	4 (3.3)
	IgM/kappa restricted	2 (1.7)
	IgA/kappa restricted	2 (1.7)
Peak within the Beta region (13)	IgM /kappa restricted	3 (23.1)
	IgG/kappa restricted	5 (38.5)
	IgG/lambda restricted	3 (23.1)
	IgD or IgE (others)	2 (15.4)
Peak at Beta-Gamma junction (4)	IgG /kappa restricted	2 (50)
	IgM/lambda restricted	2 (50)
Peak within the Alpha region (2)	IgG/ kappa restricted	2 (100)
Normal (5)	IgG /kappa restricted	4 (80)
	IgM / lambda restricted	1 (20)
Total		143 (100)

DISCUSSION

In this study, 143 patients with MM were included, with a mean age of 63.43 years. Males represented 64.3% of the cohort, and females 35.7%. This age and gender distribution is consistent with previously published data; for example, Fadel et al. and Reeta et al.[9] reported similar male predominance and mean age ranges. MM is predominantly a disease of older adults, with over 96% of cases occurring after age 45, reflecting the cumulative genetic and environmental risk factors associated with aging.[10] Our analysis showed abnormal SPE results in 96.5% of patients. The M-protein spike was most frequently located in the gamma region (83.2%), followed by the beta (9.1%) and alpha regions (1.4%). This aligns closely with Zhu et al.[11], who reported 96.2% positivity and a predominance in the gamma region. Lower detection rates reported in other studies.[12-14] may be explained by the inclusion of non-MM patients or the use of less sensitive detection techniques. Additional studies confirm the gamma-region predominance, including Reeta et al.[9] (75.9%), Dash et al. (89%), Chopra et al.[15] (84.8%), and Kapadiya et al.[12] (90.9%). Notably, Dutta et al.[10] reported more frequent beta-region spikes (80%), which may be attributed to a higher proportion of IgA paraproteins in their cohort, consistent with the known migration pattern of IgA in SPE. This variation emphasizes that paraprotein migration patterns can differ based on immunoglobulin subtype distribution within populations. Radiological evaluation revealed multiple bony lesions in 70.59% of patients, solitary lesions in 9.15%, and normal imaging in 20.26%. These findings mirror those reported by Reeta et al.9 who associated the presence of an M-band with lower hemoglobin levels and elevated ESR, calcium, and creatinine, further reinforcing the systemic impact of paraproteinemia in MM. IFE identified IgG kappa as the most frequent subtype (71.3%), followed by IgG lambda (17.5%). This distribution is consistent with the results of Zhu et al. and Dutta et al.[10] confirming the high sensitivity of IFE in detecting and classifying monoclonal proteins. Our analysis also showed significantly higher serum calcium in the IgA kappa group (mean: 12.45 mg/dL, $p = 0.020$), while hemoglobin differences among subtypes were not statistically significant. This suggests a potential association between immunoglobulin subtype and biochemical parameters, which warrants further research. For instance, a study by Rathnakumar et al.[16] found elevated calcium levels in 27 out of 90 multiple myeloma patients, though the difference was not statistically significant. Additionally, Mennens et al.[17] isolated calcium-binding IgA κ paraproteins in a patient with pseudohypercalcemia, suggesting a potential link between immunoglobulin subtype and calcium metabolism. These findings support a potential association between immunoglobulin subtype and biochemical parameters. Overall, our findings reinforce the utility of SPE as a valuable initial screening tool for paraproteinemia in suspected MM cases. IFE provides additional benefits through precise identification of immunoglobulin subtypes. The predominance of IgG kappa observed in this cohort aligns with global epidemiological data. Importantly, patients with IgA isotype MM demonstrated more severe biochemical

derangements, including higher serum calcium levels, which may have prognostic implications. The high prevalence of multiple bony lesions underscores the substantial skeletal burden of MM, consistent with previous radiological studies. Taken together, these results highlight the importance of integrating electrophoretic, immunochemical, and radiological assessments for comprehensive disease characterization and potential risk stratification.

CONCLUSIONS

Serum protein electrophoresis is a useful initial screening tool for detecting paraproteinemia, but it lacks sensitivity for accurately characterizing monoclonal proteins. Immunofixation, by contrast, provides higher sensitivity and allows precise identification of monoclonal immunoglobulin subtypes. In our cohort, IgG kappa was the predominant subtype, aligning with global trends, whereas patients with the IgA isotype exhibited more severe laboratory abnormalities.

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