Asian Pacific Journal of Cancer Care
Vol 8 No 4 (2023), 685-689
Original Research

Correlation of Plasma Cell Percentage and Monoclonal Gammapathies with Biochemical Parameters in Multiple Myeloma Patients: A Retrospective Study

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Background and objective: Multiple myeloma is characterized by the uncontrolled proliferation of monoclonal plasma cells in the bone marrow, leading to the production of non-functional intact immunoglobulin chains. This retrospective study aimed to investigate the correlation between plasma cell percentage (below 60% and above 60%) in different types of monoclonal gammapathies (IgA, IgG) and various biochemical parameters.

Materials and Methods: This analysis was conducted at the Division of Biochemistry in the Malabar Cancer Centre, a tertiary care cancer center in Kerala, India. A total of 89 patient case reports were reviewed, with complete treatment data available for 60 patients. The study evaluated the relationship between plasma cell percentage (below 60% and above 60%) in different types of monoclonal gammapathies (IgA, IgG) and various biochemical parameters.

Results: The majority of patients enrolled in the study were over 60 years of age, with more men than women included. Among the studied parameters, a significant increase in plasma protein level was observed in the group with a plasma cell percentage below 60% and IgG type monoclonal gammopathy (P value = 0.014, $p < 0.05$). Additionally, a significant elevation in WBC count was observed in patients with a plasma cell percentage below 60% and IgG type MM compared to IgA type MM patients ($p = 0.023$, $p < 0.05$). However, no significant changes were observed in plasma protein level, liver enzyme activity, renal function, serum electrolytes, CBC, and calcium level between patients with plasma cell percentages above and below 60% in multiple myeloma.

Conclusion: This study found that only a few biochemical and hematological parameters showed significant deviations between plasma cell percentages above and below 60% in different types of monoclonal gammapathies in multiple myeloma patients.

Introduction

Multiple myeloma (MM) is a mostly incurable malignant disorder of plasma cells. Premalignant plasma cell disorders are asymptomatic and are usually discovered during investigations for unrelated symptoms or laboratory abnormalities. Previous studies have substantially underestimated the true proportion of MM patients with a preexisting plasma cell disorder [1]. The bone marrow contains healthy plasma cells, which play a significant role in the immune system. Multiple cell types make up the immune system and collaborate to combat infections and other

disorders [2]. Lymphocytes, including T cells and B cells, are the major immune cells in our body. They can be found throughout the body, including lymph nodes, bone marrow, intestines, and circulation. B cells develop and transform into plasma cells in response to an infection. Plasma cells, upon maturation, produce immunoglobulins, commonly known as antibodies, which aid the body in battling and eliminating pathogens [3]. In addition to plasma cells, normal bone marrow serves as the home for red blood cells, white blood cells, platelets [4].

The aberrant protein or antibody produced by the plasma cells goes by a variety of names, including monoclonal immunoglobulin, monoclonal protein (M-protein), M-spike, and paraprotein [5]. According to research reported in The Lancet Haematology, the incidence of multiple myeloma (MM) is increasing globally. The prevalence of MM is rising, especially among men over 50. The Age Standardized Rate (ASR) for MM incidence was 1.78 per 100,000 individuals worldwide in 2020. Males were more likely than women to develop MM (ASR: 2.10), and men were also more likely to die from MM (ASR: 1.41) than women (ASR: 0.93) [6].

The overproduction of plasma cells in the bone marrow of patients with multiple myeloma can crowd out healthy blood-forming cells and result in low blood counts. This may cause anemia, lethargy, and frailty. Low platelet counts in the blood, known as thrombocytopenia, can also occur in multiple myeloma, leading to increased bleeding and bruising. Multiple myeloma prevents the production of antibodies to combat infection because the myeloma cells push out the healthy plasma cells. The antibodies produced by myeloma cells are ineffective in preventing infections. Additionally, myeloma cells interfere with bone-strengthening cells since bones are continually rebuilt to maintain their strength [7].

The symptoms of myeloma are described as “CRAB,” with each letter corresponding to a symptom. Increased calcium levels, greater than 0.25 mmol/L above the upper limit of normal or a level greater than 2.75 mmol/L, are represented by the “C” in CRAB. Renal problems, identified by a creatinine level higher than 173 mmol/L, are represented by the “R” in CRAB. Anemia, defined as a low hemoglobin level less than 10 g/dL, corresponds to the “A” in CRAB. Bone lesions, including lytic lesions and osteoporosis, are represented by the “B” in CRAB. If CRAB features are absent, having more than 60% of the cells in the bone marrow as plasma cells can be considered a symptom of MM [8].

The present study aims to investigate the pattern of different biochemical parameters in cases with plasma cell percentages below and above 60%, as well as the significant differences in biochemical parameters associated with different types of gammapathies in both above and below 60% plasma cell types of MM.

Materials and Methods

The present study is a retrospective observational analysis of patients diagnosed with multiple myeloma between January 1, 2016, and December 31, 2016, at Malabar Cancer Centre in Kerala, India. Since there were no ethical issues in this study, we could easily proceed with the necessary formalities. The study was approved by the Institutional Review Board of Malabar Cancer Centre, and data were obtained from the Cancer Registry and Medical Records division. We consecutively analyzed the case reports of 89 patients who were diagnosed with multiple myeloma during the study period. We specifically focused on newly diagnosed multiple myeloma patients with complete laboratory data available in their medical records. After a thorough analysis of the case reports, we excluded 29 patients due to incomplete laboratory test results.

Blood samples were collected and separated into serum for biochemical assays. We evaluated the relationship between plasma cell percentage (below 60% and above 60%) and various biochemical parameters, including calcium, albumin, globulin, total protein, LDH, β2 microglobulins, ALP, AST, ALT, hemoglobin, urea, creatinine, sodium, potassium, and blood cell parameters such as RBC,

WBC, monocyte, basophile, eosinophil, and lymphocyte. Biochemical analysis was performed using the Vitros 5600 Dry Chemistry integrated system (Ortho Clinical Diagnosis, USA) with commercial kits following the manufacturer's protocol. For complete blood cell analysis, blood samples were collected in EDTA-K2 anticoagulant tubes and analyzed using the LH 780 Analyzer (Beckman Coulter, USA) based on the Coulter principle and electrical impedance. Serum protein electrophoresis and immunofixation were conducted using the Helena SAS-3 SAS-4 system (Helena Biosciences Europe). Plasma cell percentage was determined from bone marrow cells obtained through bone marrow biopsy.

Criteria for Analysis

Inclusion Criteria: Subjects who have been diagnosed with multiple myeloma and confirmed by the electrophoresis method with complete treatment records were included in the study.

Exclusion Criteria: Multiple myeloma patients with incomplete medical records were excluded from the study.

Statistical analysis

The statistical analysis was performed using IBM SPSS software. To assess the correlation and changes between the two types of monoclonal gammopathy in the above 60% and below 60% groups, a paired t-test was conducted. A p-value of less than 0.05 was considered statistically significant. The data were expressed as mean ± SD.

Results

The main objective of our study was to analyze the correlation between plasma cell percentage and biochemical parameters in multiple myeloma. The parameters included in the analysis were total protein, albumin, globulin, β2 microglobulin (plasma proteins), calcium level, SGOT, SGPT, LDH, ALP (liver enzymes), sodium, potassium (serum electrolytes), RBC, WBC, monocyte, lymphocyte, basophil, eosinophil, Hb (Complete Blood Count), urea, creatinine (renal function), IgA, IgG (immunoglobulins), and plasma cell percentage in patients with multiple myeloma.

For this study, we utilized the case reports of 89 patients who were treated for multiple myeloma at MCC in the year 2016. Out of these 89 case reports, we included 60 patients with complete treatment records in our analysis. The distribution of patients based on plasma cell percentage showed that 69.6% had plasma cells below 60%, while 30.4% had plasma cells above 60%.

Age and gender distribution of MM patients with above and below 60% plasma cells

The age of MM patients ranges from 45 to 75 years; the mean age was 63.07 ±9.88 years; out of these 58.9% were males and 41.1% were females.

Status of plasma cell percentage with overall analysis of the number of cases of monoclonal immunoglobulins

Among the complete treatment records, the number of cases of immunoglobulin (IgA, IgG) and serum light chain (Kappa, Lambda) below and above 60% of plasma cells were primarily analyzed. The collected data revealed that there were 14 cases of IgA monoclonal gammopathy below 60% and 4 cases above 60%. In the case of IgG monoclonal gammopathy, there were 25 cases below

60% and 3 cases above 60%. Furthermore, for free light chains kappa and lambda, there were 22 cases below 60% and 17 cases above 60% for kappa light chain, and 17 cases below 60% and 14 cases above 60% for lambda light chain.

Comparison of biochemical parameters in MM Patients with above and below 60% plasma cell group

Plasma protein levels-

In plasma cell below and above 60% category of MM patients plasma proteins total protein, albumin, globulin and β2 microglobulinlevels were compared. A significant rise was observed in the plasma protein level of β2 microglobulin (P value= 0.014, $p<0.05$) however there was no significant difference were observed in other proteins (Table 1).

Parameters	Plasma cells 60% elow	Plasma cells 60% above	P value
Total Protein (g/dl)	8.1 ±2.1	8.3 ±3.1	0.966
Albumin (g/dl)	4.5 ± 5	3.9 ± 0.9	0.62
Globulin (g/dl)	4.4 ± 2.1	3.9 ± 2.5	0.407
β- 2 Microglobulin (mg/L)	5665.7 ± 38.5	11923 ± 143.2	0.014*

Table 1. Level of Plasma Proteins in 60% Below and Above Plasma Cell Cases of MM Patients.

Values are expressed as Mean ±SD. * indicates the significance P≥ 0.05

Liver enzymes-

Liver enzymes such as ALP, SGOT, SGPT and LDH were compared between above and below 60% plasma cell group. No significant changes were observed in liver enzyme activity ($p\geq0.05$) (Table 2).

Parameters (IU/L)	Plasma cells 60% below	Plasma cells 60% above	P value
ALP	111.7 ±77.8	86.2 ±25.6	0.274
SGOT	37.1 ±22.4	30.6 ± 15.6	0.302
SGPT	40.0 ±35.2	32.5 ± 28.1	0.479
LDH	551.7 ± 375.3	448.2 ± 227.8	0.396

Table 2. Level of Liver Enzymes in 60% Below and Above Plasma Cell Cases of MM Patients.

Values are expressed as Mean ±SD. * indicates the significance P≥ 0.05

Renal function Tests-

Urea and creatinine values were compared for between above and below 60% plasma cell group and found both values were not significant ($p\geq0.05$).

Serum electrolytes-

Serum sodium and potassium levels were compared between the 60% above and below plasma cells groups. There was no significant difference between the groups ($p\geq0.05$).

Calcium level-

The difference of calcium levels in the 60% above and below plasma cells groups was found not significant two groups of MM (p≥0.05 (Table 3).

Parameters	Plasma cells 60% below	Plasma cells 60% above	P value
Urea (mg/dl)	39.0 ± 4.8	24.1 ± 16.	0.243
Creatinine (mg/dl)	2.3 ± 3.6	1.5 ± 1.4	0.381
Sodium (mmol/L)	142.2 ± 35.2	138.8 ± 2.2	0.695
Potassium (mmol/L)	4.1 ± 1.5	4.5 ± 0.8	0.435
Calcium (mg/dl)	9.5 ± 1.8	8.4 ±1.8	0.067

Table 3. Renal Function Tests, Serum Electrolytes and Calcium Level in 60% Below and Above Plasma Cell Cases of MM Patients.

Values are expressed as Mean ±SD. * indicates the significance P≥ 0.05. No significant changes observed

Comparison of complete blood cells in MM Patients with above and below 60% plasma cell groups

Parameters in complete blood count were compared with MM Patients with above and below 60% plasma cell groups. There was no significant difference found in RBC, WBC, monocyte, basophil, eosinophil, lymphocyte count between above and below 60% plasma cell groups of MM (p≥0.05) (Table 4).

Parameters	Plasma cells 60% below	Plasma cells 60% above	P value
RBC (x103/µl)	3.24±1.45	2.7±0.60	0.37
WBC (x103/µl)	6.98±3.57	4.69±1.50	0.17
Monocyte %	10.12±15.10	7.80±6.70	0.6
Basophyl %	0.34±0.61	0.30±0.40	0.92
Eosinophylv%	1.98±2.70	1.90±2.60	0.99
Lymphocyte %	30.17±12.8	30.40±18.70	0.37
Hb (g/dl)	10.40±2.10	8.6±1.70	0.12

Table 4. Complete Blood Cell Count in 60% Below and Above Plasma Cell Cases of MM Patients.

Values are expressed as Mean ±SD. * indicates the significance P≥ 0.05. No significant changes observed

Comparison of plasma proteins in different types of monoclonal gammopathy MM Patients with above and below 60% plasma cell groups

The levels of total protein, albumin, globulin and beta 2 microglobulin were compared in IgG and Ig A types monoclonal gammopathy. The difference between the MMs were found not significant in above and below 60% plasma cell groups. The level of β-2 microglobulin (3652±214 for Ig A and 5034±4146 mg/L) in below 60% plasma cell gammapathies were not significantly changed with above 60% (5008±307.5 for Ig A and 13898.5±10857 for Ig G) plasma cell cases (p≥0.05).

Comparison of liver enzymes in different types of monoclonal gammopathy MM Patients with above and below 60% plasma cell

groups

The levels of ALP, SGOT, SGPT and LDH were compared in IgG and Ig A monoclonal gammopathy. The difference between the MMs were found not significant in above and below 60% plasma cell groups (p≥0.05).

Comparison of renal function tests in different types of monoclonal gammopathy MM Patients with above and below 60% plasma cell groups

The levels of urea and creatinine were compared in IgG and Ig A monoclonal gammopathy. The difference between the MMs were found not significant in above and below 60% plasma cell groups (p≥0.05).

Comparison of serum electrolytes in different types of monoclonal gammopathy MM patients with above and below 60% plasma cell groups

The levels of sodium and potassium were compared in Ig G and Ig A monoclonal gammopathy. The difference between the MMs were found not significant in below 60% plasma cell groups (p≥0.05).

Comparison of complete blood count in different types of monoclonal gammopathy MM patients with above and below 60% plasma cell groups

The levels of Parameters in complete blood count were compared compared in IgG and Ig A monoclonal gammopathy. There was no significant difference found in RBC, monocyte, basophil, eosinophil, lymphocyte count between above and below 60% plasma cell groups of MM (p≥0.05). It was found the difference in total WBC count between different types of MM was statistically significant in below 60% plasma cell group (P=0.023) (P<0.05). The p value for difference in WBC count wasfound so this is statistically significant.

Discussion

Patients included in the current study constituted a representative sample of the population of multiple myeloma patients, with an age range of 30 to 79 years. Among these patients, 58.9% were males and 41.1% were females. A standardized protocol for diagnosis and treatment was followed for all patients. The objective of the study was to evaluate the correlation between plasma cell concentration above 60% and below 60% in different types of monoclonal gammopathies. Age, gender, and their correlation with plasma cell percentage were retrospectively obtained from the clinical records. The current diagnostic criteria for multiple myeloma require the presence of end-organ damage known as the CRAB criteria, which includes hypercalcemia, renal dysfunction, anemia, and destructive bone lesions. However, patients without CRAB features may still receive treatment if they have a bone marrow plasma cell percentage greater than 60% [9]. Monitoring of biochemical and clinical parameters in multiple myeloma is an important area of investigation among cancer researchers.

The present study aimed to analyze the correlation between different immunoglobulin groups and plasma cell percentage (<60% and >60%) with various biochemical parameters in multiple myeloma. Among these parameters, a significant increase in plasma protein level, particularly β-2 microglobulin, was observed in patients with plasma cell percentage above 60% (p<0.05). Previous

studies have also shown that β-2 microglobulin levels increase in early and risk stages of multiple myeloma, indicating its diagnostic and prognostic significance [10]. In the present study, the activity of β-2 microglobulin was significantly higher in patients with above 60% plasma cells compared to the below 60% plasma cells group.

The correlation between 60% plasma cells and immunoglobulins, specifically IgA and IgG gammopathies, was also examined. There was a significant elevation in WBC count in IgG compared to IgAin patients with plasma cell percentage below 60% in multiple myeloma ($p<0.05$). This finding suggests a strong correlation between WBC count and immunoglobulin type (IgG compared to IgA) in patients with below 60% plasma cells. However, there is limited research in this area.

Another important finding is that multiple myeloma cases with 60% plasma cells were more common in patients above 60 years of age. This finding aligns with previous studies that have shown an increased incidence of multiple myeloma in older patients [11]. Furthermore, the study found a higher prevalence of multiple myeloma in men compared to women, which is consistent with existing research, although the exact reasons behind this gender disparity remain unclear.

Limited studies have been conducted on the correlation between plasma cell percentage and various biochemical parameters such as plasma protein, serum electrolytes, urea, creatinine, liver enzymes, complete blood count, and calcium [12]. The present retrospective study had certain limitations in data collection, resulting in a sample size of only 60 cases of multiple myeloma, which may have impacted the completeness of the study. Therefore, further research is necessary to explore the correlation between plasma cell percentage and different biochemical parameters in multiple myeloma, with a focus on detailed data collection.

The prompt and accurate diagnosis of multiple myeloma is crucial for initiating appropriate treatment. Hematologists and clinicians should collaborate to achieve early diagnosis and prompt management of patients. The present study highlights the importance of biochemical parameters such as plasma protein, urea, serum electrolytes, liver enzymes, complete blood count, and immunoglobulins in monitoring multiple myeloma.

In conclusion, the current study concludes that age above 60 has the greatest impact on multiple myeloma (MM), and men are more affected by MM compared to women. Most plasma protein levels did not show significant changes, except for β-2 microglobulin, and only the total white blood cell (WBC) count exhibited a significant difference among different types of MM cases based on plasma cell percentage.

Conflict of interest

The Authors declares that they have no conflicts of interest to disclose.

Acknowledgments

Authors are thankful to Dr. Sangeetha K Nayanar, HOD, Department of Clinical Laboratory Services and Translational Research, Malabar Cancer Centre who provided valuable suggestions throughout the research. This research work did not receive any specific research grant from funding agencies in the public commercial or not-for-profit sectors.

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