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Correlation Between β2-Microglobulin, Grobulin Levels & The Number of Plasmatic Cells in Patients with Multiple Myeloma

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ABSTRACT

Introduction: *Multiple myeloma is multifocal neoplasia of plasmatic cells that affects the bone marrow. It is associated with the production of a urinary or serum protein. It represents approximately 1 percent of cancer cases worldwide and between 10 to 15 percent of all cases of hematological malignancy. Furthermore, it has been proposed that the β2-microglobulin levels are correlated with other factors that can predict multiple myelomas such as the number of plasmatic cells and the creatine levels.*

Goals: *To determine the correlation between β2-microglobulin, globulin levels, and the number of plasmatic cells in patients with multiple myeloma.*

Methods and techniques: *We conducted an observational, retrospective, transversal, and analytical study in the Hospital of the Mexican Institute of Social Security at the Veracruz Port. Our population analyzed comprehended 45 patients between the ages 30 and 80 with a confirmed diagnosis of multiple myeloma. We measured the β2-microglobulin levels and globulin levels, and the number of plasmatic cells during the diagnosis of patients. Furthermore, we conducted a statistical analysis using a Pearson correlation.*

Results: *The average age was 61 years with a margin of error of 11.48 years. The myeloma of IgG type was the one of major prevalence and represent 82.2 percent. It was followed by the IgA type and the IgM type, which represented 15.5 and 2.2 percent respectively. The Pearson correlation coefficient (Pearson's r) between the β2-microglobulin levels and globulin levels was 0.92. The Pearson's r between the number of plasmatic cells and β2-microglobulin, excluding patients with high serum creatine levels (i.e. larger than 1.2 mg/dl), was 0.371.*

Conclusions: *The predominant type of myeloma in the analyzed population was the IgG type. Furthermore, this myeloma affected mainly men in our study. The average age was 61 years with a margin of error of 11.48 years when compared to other populations in our study.*

Keywords

Multiple myeloma, Globulin, Plasmatic cells.

Introduction

Multiple myeloma is a malignant disease that consists in the spread of clonal plasma cells in the bone marrow. This proliferation is typically accompanied by the secretion of monoclonal immunoglobulins, which are detectable in urine or serum [1,2]. Multiple myeloma represents about 1 percent of all cases of cancer in the world and between 10 to 15 percent of haematological malignancies. It is second only to lymphoma as the most common haematological malignancy, and it is the 10th leading cause of death

from cancer (3.8 deaths per 100,000 population). Controlling for age, 6.9 in 100,000 men and 4.5 in 100,000 women suffer from this disease. Furthermore, environmental aspects may interact with genetic factors to increase the risk of multiple myeloma. On average, men tend to develop this disease at 71 while women at 74 [3].

The risk of suffering from multiple myeloma increases with the age. It is rare for people under 45 to develop this disease (they only represent 2% of the cases). The survival rate after 5 years of suffering the disease was 45 percent between 2009 and 2010. The etiology of this disease remains unknown. Factors that can increase the risk of developing multiple myeloma include ionizing radiation, pesticides, benzol, obesity, and chronic infection [4-6].

Beggars and Bearn isolated for the first time the serum beta 2 microglobulin (β2-m) from the urine of the patients suffering from proximal renal tubular disorders. The generation and secretion of β2-m are constant and low among healthy individuals. Due to its small size, β2-m is filtered by the glomerular membrane, but it is later reabsorbed by proximal tubule cells [7-9].

In Mexico, the statistical and epidemiological information is limited. According to the Mexican guide of multiple myeloma, this disease represents between 4.2 and 7.7 percent of all cases of onco-hematological diseases. This number, however, only corresponds to the cases of one health facility. The analysis was conducted over 20 years on patients diagnoses with MM in the center of hematology and internal medicine of Puebla. Between 1983 and 2003, 66 patients were diagnosed with MM. Over this period, a total of 9,120 patients were observed, including 855 people with hematologic malignancy. MM represented 7.7 percent of all the cases of hematological malignancy [10-13].

A monoclonal protein (M) in the urine is a symptom of MM. However, this sign is only visible in 82 percent of the patients; serum protein electrophoresis procedure is necessary. For patients suspected of having MM, the recommended screening methods are a rearranging of serum protein electrophoresis, serum immunofixation, serum-free light chain (FLC) testing, and a 24-hour serum protein electrophoresis with immunofixation. The type of M protein is IgG in 50 percent of the cases, IgA in 20 percent, IgD in 2 percent, and IgM in 0.5 percent [14,15].

The main purpose of this analysis is to determine the correlation between the serum beta 2 microglobulin (β2-m), globulins, and the quantity of plasmatic cells in patients with multiple myeloma.

Methods and Techniques

This study was observational, retrospective, transversal, and analytical. It was conducted in the Hospital of the Mexican Institute of Social Security in the Veracruz Port. It includes 45 patients 30 to years old with a confirmed diagnosis of multiple myeloma. Our study measured the values of β2-microglobulin, globulin, and the number of plasmatic cells. While conducting the diagnosis IgG, IgE, and IgM, we obtained the numbers reported in the study of 24-hour serum protein electrophoresis procedure with immunofixation, total protein measurement, and bone marrow aspiration respectively.

Statistical analysis: the results of the analysis of our hypothesis were calculated using the statistical package Minitab. We employed a multiple linear regression and Person correlation. Correlation between plasmatic cells and β2-microglobulin. Correlation between plasmatic cells and globulins. Correlation between β2-microglobulin and globulins.

Results

By sex, there are 25 male cases and 20 female cases, which represents 55.5 and 45.5 percent respectively of all the cases. The early average age was 61 with an 11.48 margin of error. The maximum age was 82 years and the minimum 31. The most prevalent type of myeloma was the IgG with 37 cases. It was followed by the IgA type with 7 cases, and the IgM type with 1 case. These types of myeloma represented 82.2, 15.5, and 2.2 percent respectively. The value of serum creatine was included as a variable of interest because its high concentration significantly increased the concentration of β2-microglobulin. Of the total number of patients, 44.4 percent showed alterations in the levels of serum creatine and creatine with values higher than 1.2 and less than 1.2 milligrams (mg) per deciliter (dL) respectively (Table 1).

We observed a high correlation between the analyzed variables due to the higher concentrations of β2-microglobulin among patients with values of serum creatin higher than 1.2 mg/dc. Therefore, we conducted a second analysis excluding those patients with a higher concentration of serum creatin (n=25) and we obtained a similar correlation between the analyzed variables. A Pearson correlation coefficient of 0.92, which is statistically significant at the 1 percent suggests a positive correlation between the levels of β2-microglobulin and the levels of globulin (Tables 2 and 3) (Figures 1 and 2).

Table 1: Characteristics of patients with Multiple Myeloma.

	Frequency (n = 45)	Percentage
Sex		
Masculine Feminine	25 20	55.56% 44.44%
Types of Myeloma		
IgA	7	15.56%
IgG	37	82.22%
IgM	1	2.22%
Serum Creatinine		
with alterations >1.2 mg/dl.	20	44.44%
without alterations <1.2 mg/dl.	25	55.56%

Table 2: Plasma cells and β-2 microglobulin correlation in patients with Multiple Myeloma.

Variables	β-2 microglobulin (n=45)	β-2 microglobulin Serum creatinine>1.2mg/dl (n=25)
Plasma cells	r = 0.093 (p = 0.544)	r = 0.317 (p = 0.123)

Pearson correlation *p < 0.05

Table 3: Plasma cells and β-2 microglobulin correlation with globulins in patients with Multiple Myeloma.

Variables	Globulins (n=45)	Globulins Serum creatinine>1.2mg/dl (n=25)
Plasma cells	r = 0.022 (p = 0.887)	r = 0.388 (p = 0.05)
β-2 microglobulin	r = 0.92 (p = 0.0001)*	r = 0.91 (p = 0.0001)*

Pearson Correlation *p<0.05

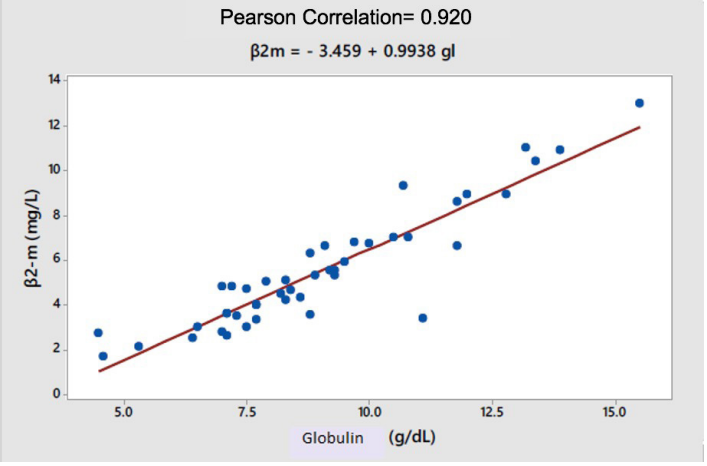

Figure 1: β-2 microglobulin (mg / L) and globulin (g / dl) correlation in Multiple Myeloma with Serum creatinine <1.2mg / dl.

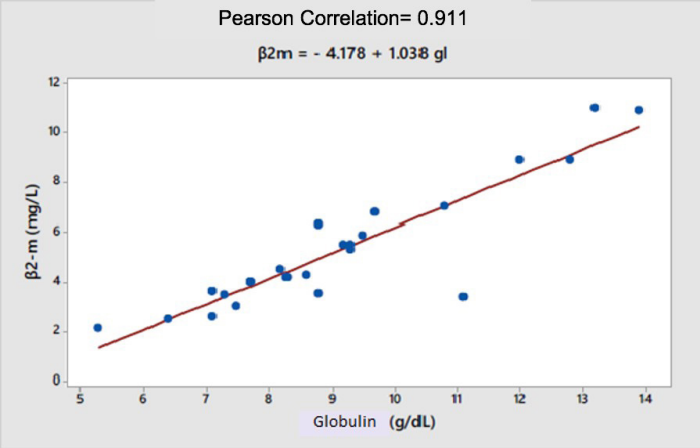

Figure 2: β-2 microglobulin (mg / L) and globulin (g / dl) correlation in Multiple Myeloma with Serum creatinine> 1.2mg / dl.

Discussion

Regarding the analyzed epidemiological variables, our results indicates that the myeloma of major prevalence was the IgG type, which concurs with the results of Rajkumar [15]. The average age at diagnosis was 61 with a margin error of 11.48 years, which is a similar value to the one suggested by Gerecke, 72 years [16]. In accordance to the results of the work of Konrad C.N et al., we found that this disease is more prevalent among men; 55.5 percent of the cases were male [17].

While the β2-microglobulin is a widely studied factor that can predict multiple myeloma, existing research has not analyzed its possible interaction with other factors that can also cause the tumor load. Among these factors, we can mention the number of plasmatic cells in the marrow bone and the levels of globulin, which exhibit a direct correlation with the immunoglobulins secreted by the plasmatic cell, prevalent in myeloma. Thus, we rely on the Pearson correlation to analyze the interaction and the degree of correlation in our variables of interest: number of plasmatic cells, β2-microglobulin, and globulin levels.

An intersting finding that deserves to be mentioned is that we observed that the levels of β2-microglobulin increased disproportionately among the patients suffering kidney failure, i.e. patients who initially had levels of serum creatine higher than 1.2 mg/dl [18].

On the other hand, the correlation between the levels of β2-microglobulin and the number of plasmatic cells was very low and statistically insignificant. This finding concurs with the results of Greip et al. [19] In their study, the number of plasmatic cells varied independently to microglobulin levels. However, a small number of plasmatic cells predicted a greater chance of survival among patients with myeloma even though there was no direct correlation between the levels of β2- microglobulin and the plasmatic cells [20].

Among the analyzed variables, only β2-microglobulin levels and globulin levels exhibited a positive correlation, large in magnitude (Pearson = 0.92) and statistically significant at the 1 percent. This finding differs from the results from the work of Bataile that suggests that the correlation between the β2-microglobulin levels and the levels of the M components of IgA or IgA was not significant. In Bataille's study, approximately 12 percent of the analyzed patients with myeloma IgG or IgA showed normal or subnormal β2-microglobulin levels. Based on the results of our study, however, we can argue that both the individual and combined levels of IgG and IgA are good predictors of myeloma.

High globulin levels, for instance, suggest the existence of monoclonal gammopathy, as the results of the work of Bora K. et al. suggest. This study concludes that 76 percent of the patients with monoclonal gammopathy also suffered from multiple myeloma; they exhibited initial serum globulin levels greater than 4 mg/dl.

Conclusion

The results obtained in our study suggest that the type of predominant myeloma in the analyzed population was the IgG type. Men were more affected than women by this malignant disease. The early average age was 61 years, with a margin of error of 11.48 years when compared to other populations in our study.

We found a positive correlation between the β2-microglobulin levels and globulin levels, large in magnitude. This finding allowed us to establish a functional model for a hematologist in charge of the initial diagnosis of patients with multiple myeloma.

The current study allowed us to analyze biochemical factors correlated with multiple myeloma and determine a statistical significance to establish a prognosis of survival in patients suffering from this malignant disease.

References

1. Kumar SK, Rajkumar SV, Kyle RA, et al. Multiple myeloma. Nat Rev Dis Primers. 2017; 3: 17046.
2. Röllig C, Knop S, Bornhäuse M, et al. Multiple myeloma. The Lancet. 2015; 385: 2197-2208.
3. Mann H, Katiyar V, Varga C, et al. Smoldering multiple myeloma - Past, present, and future. Blood Rev. 2021; 100869.
4. Gerecke C, Fuhrmann S, Strifler S, et al. "The Diagnosis and Treatment of Multiple Myeloma." Deutsches Ärzteblatt International. 2016; 113: 470-476.
5. Nomura T, Huang WC, Zhau HE, et al. "β2-Microglobulin-Mediated Signaling as a Target for Cancer Therapy." Anti-Cancer Agents in Medicinal Chemistry. 2014; 14: 343-352.
6. Hanbali A, Hassanein M, Rasheed W, et al. The Evolution of Prognostic Factors in Multiple Myeloma. Advances in Hematology. 2017; 20: 1-11.
7. Štifter S, Babarović E, Valković T, et al. Combined evaluation of bone marrow aspirate and biopsy is superior in the prognosis of multiple myeloma. Diagnostic Pathology. 2010; 5: 156-200.
8. Svatoňová J, Bořecká K, Adam P, et al. Beta2-Microglobulin as a Diagnostic Marker in Cerebrospinal Fluid: A Follow-Up Study. Hindawi Publishing Corporation. 2014; 20: 1-6.
9. Bataille R, Grenier J, Sany J. Beta-2 Microglobulin in Myeloma: Optimal Use for Staging, Prognosis, and Treatment-A Prospective Study of 160 Patients. Blood. 1984; 63: 468-476.
10. Ruiz A.G, Gómez-Rangel JD, Ruiz-Delgado GJ, et al. Multiple Myeloma in Mexico: A 20-Year Experience at a Single Institution. Archives of Medical Research. 2004; 35: 163-167.
11. Morales S.A, Martinez R.A. Frecuencia del mieloma múltiple en el Hospital Regional General Ignacio Zaragoza, ISSSTE. Revista de Especialidades Médico-Quirúrgicas. 2008; 13: 99-103.
12. Cano C.R, Cedillo C.J.L, Garcés R.O, et al. Guias Mexicanas de diagnostico y recomendaciones terapeuticas para mieloma multiple 2013. Revista de Hematologia. 2013; 11: 46-62.
13. Alvarado I.M, Álvarez V.J.L, Anaya C.I, et al. Primer Consenso Nacional de Mieloma Múltiple por Hematólogos del ISSSTE. Revista de Hematologia de Mexico. 2015; 16: 306-332.
14. Rajkumar S.V. Multiple myeloma: 2016 update on diagnosis, risk-stratification, and management. American Journal of Hematology. 2016; 91: 719-734.
15. Rajkumar S.V, Kumar S. "Multiple Myeloma: Diagnosis and Treatment." Mayo Clinic proceedings. 2016; 91: 101-119.
16. Pineli M, Pinho W, Amigo C, et al. Multiple Myeloma: Epidemiology and Burden of Disease Analysis in Latin America. Value in Health. 2017; 20: 32-35.
17. Konrad C.N, Lewis W.D. Multiple Myeloma: Diagnosis and Treatment. American Family Physician. 2014; 78: 417-422.
18. Argyropoulos CP, Chen SS, Ng Y-H, et al. Rediscovering Beta-2 Microglobulin As a Biomarker across the Spectrum of Kidney Diseases. Frontiers in Medicine. 2017; 4: 73.
19. Greipp P.R. et al. Value of beta 2-Microglobulin Level and Plasma Cell Labeling Indices as Prognostic Factors in Patients with Newly Diagnosed Myeloma. Blood. 1988; 72: 219-223.
20. Bora K, Das U, Barman B, et al. Monoclonal gammopathy with double M-bands: An atypical presentation on serum protein electrophoresis simulating biclonal gammopathy. Indian J Pathol Microbiol. 2017; 60: 590-592.